CLINICOETIOLOGICAL STUDY OF STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS SPECTRUM AND THE CORRELATION OF SCORTEN WITH PROGNOSIS

Dissertation submitted in partial fulfilment of the

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TIRUNELVELI MEDICAL COLLEGE HOSPITAL

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY,

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I solemnly declare that the dissertation titled **"CLINICOETIOLOGICAL STUDY OF STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS SPECTRUM AND THE CORRELATION OF SCORTEN WITH PROGNOSIS"** was done by me at Tirunelveli Medical College, Tirunelveli–627011, during the period January 2016 to June 2017 under the guidance and supervision of **Dr K Punithavathi, MD**, to be submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of MD DEGREE in DERMATOLOGY, VENEREOLOGY & LEPROSY, BRANCH-XX.

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CONTENTS

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Dr. Amuthavalli.K

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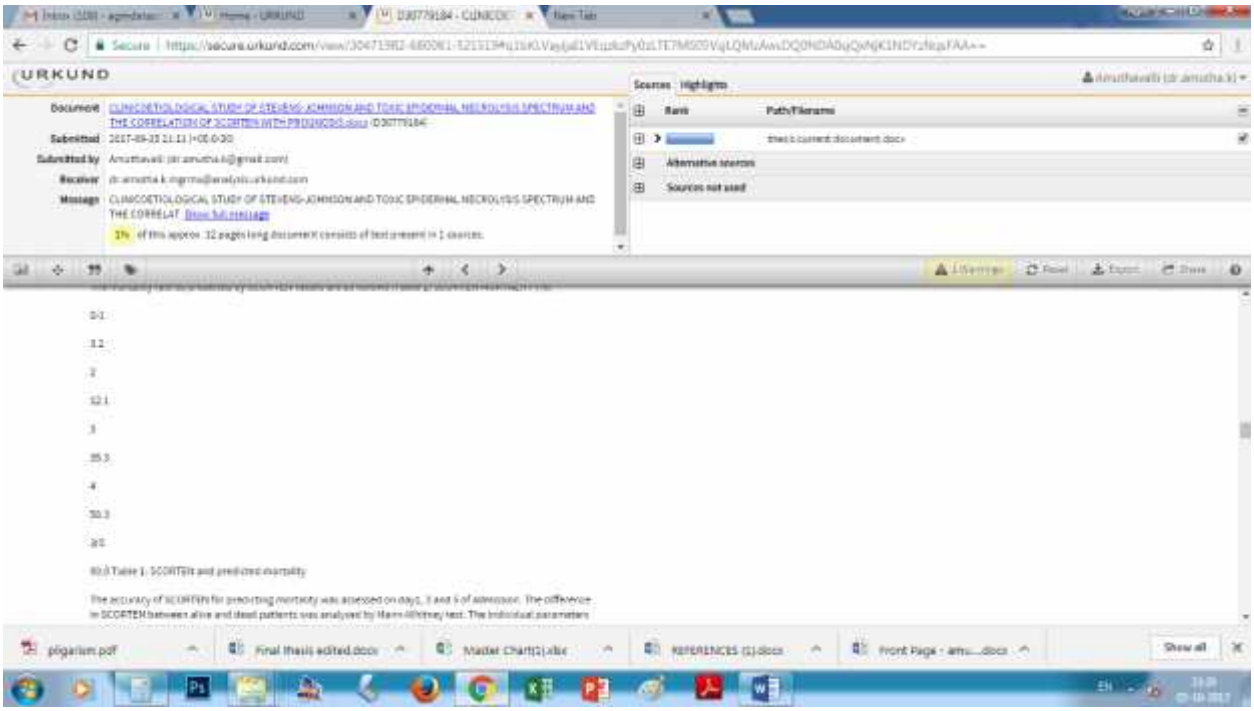
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PRINCIPAL INVESTIGATOR: DR.K.AMUTHAVALLI, MBBS.,

DESIGNATION OF PRINCIPAL INVESTIGATOR JUNIOR RESIDENT I YEAR IN DERMATO VENEREO LEPROLOGY

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THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
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9.	Investigator's Agreement with Sponsor	☐
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BACKGROUND

Adverse drug reactions (ADR) are commonly encountered in day to day clinical practice. They are unintended and harmful responses to medicines that occur in doses normally used for the prophylaxis, treatment or the diagnosis of the disease. Many such ADRs presents with cutaneous signs.[1] They are frequently seen with drugs commonly used in general practice like sulfonamide antibiotics, aminopenicillin, cephalosporins, quinolones, aromatic anticonvulsants, NSAIDS of Oxicam group. Cutaneous ADR ranges from benign ADR like acute exanthem, pruritus, eczema, photosensitivity, urticaria, angioedema, anaphylaxis, lichenoid and Fixed drug eruption pigmentation, drug induced erythema nodosum, pityriasis rosea and acneiform eruption, to the severe cutaneous ADR like, drug related eosinophilia and systemic symptoms(DRESS) , acute generalized exanthematous pustulosis (AGEP) , drug induced exfoliative dermatitis and Stevens Johnson and Toxic epidermal Necrolysis syndrome(SJS,TEN).[2] Recognizing the adverse drug reactions needs knowing the various morphologies, expecting it and diagnosing it and it is of utmost importance in clinical dermatological practice.

Among the four severe cutaneous adverse drug reaction (SCAR), prognosis is good and mortality is less with AGEP, drug induced exfoliative dermatitis and DRESS in order, with SJS and TEN carrying a significant mortality.[3] Mortality rate ranges from 1-5% in SJS to 25-35% in established TEN.[4] Most patients die of

acute illness with the most common cause of death being septicemia related multi organ failure. So, finding the etiology of SJS and TEN and knowing its various clinical features is of utmost importance, in making the diagnosis at the first visit of the patient and stopping the offending drug at the earliest. The disease progression and prognosis of SJS and TEN is unpredictable, ranging from complete recovery to mortality.

Certain indicator or scoring system is of absolute necessity in predicting the prognosis in SJS-TEN patients, which will aid in deciding the modality of treatment and thus help reducing mortality in this dermatological emergency. Since, once this acute crisis phase is tided over, sequelae in terms of long term morbidity is less. Such indicators in clinical practice are SAPS II – Simplified acute physiology Score II, Burn Scoring System – (age+ percentage of BSA involved on admission) and SCORTEN. The former two are not used in clinical practice now, because both of them are tedious and non specific.[5]

SCORTEN is a scoring system for SJS and TEN developed and validated in the year 2000 in European population by Bastuji-Garin et al in patients of TEN and has been used in various parts of the world in prognostication of SJS and TEN since then.[6,7,8,9] It is based on 7 risk factors – age, presence of malignancy, extent of epidermal detachment, tachycardia, blood glucose, bicarbonate and blood urea

nitrogen(BUN) levels recorded within 24 hours of admission. A score from 1-7 predicts a probability of mortality from 3.2% to 90.0%.

Although the score is performing well, there are issues regarding its accuracy as well as its predictive power.[10,11,12] The usefulness of SCORTEN in Indian patients, whose genetic makeup is different from the European population in whom it was originally studied and the role of other factors like tuberculosis and other chronic diseases which also plays an additional role in predicting mortality is yet to be confirmed.[13,14,15] This is confirmed in our study.

About the management, various treatment like corticosteroids, intravenous immunoglobulins(IVIG), cyclosporine A and plasmapharesis have been tried with conflicting results.[12,13,16] Controversies still continue about whether conservative management including meticulous inpatient care alone or addition of immunosuppressive agent is needed for the better outcome of the patient. However no clear consensus exists on the line of management till date.

Also there have been only a few large prospective scale studies which highlight the etiological agents and clinical features of SJS and TEN especially in Indian context.[16,17,18] Also to the best of our knowledge there are no prospective published studies confirming the validity of SCORTEN in South Indian population.

In view of the above lacunae, our study aimed at studying the clinicoetiological profile and outcome of SJS-TEN patients and to confirm the accuracy of SCORTEN as a prognostic marker in South Indian patients by serial analysis on Day 1, 3 and 5 of admission.

AIMS & OBJECTIVES

PRIMARY OBJECTIVES

1. To study the various morphological patterns and etiology of Stevens Johnson Syndrome and Toxic Epidermal Necrolysis.
2. To evaluate the accuracy of SCORTEN as prognostic marker in the outcome of patients with SJS-TEN spectrum.

SECONDARY OBJECTIVES

1. To know about the demographic pattern, incidence of SJS and TEN and the percentage of occurrence of SJS and TEN among other drug reactions
2. To observe the time interval between the exposure of noxious stimuli and the development of SJS and TEN and its correlation with etiology.
3. To find out the outcome of patients in terms of morbidity and mortality.

REVIEW OF LITERATURE

INTRODUCTION

Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis(TEN) are dermatological emergencies characterized by life-threatening acute severe mucocutaneous reactions typically induced by drugs.[19] It is a systemic disease involving the sloughing of ophthalmic, pulmonary, genitourinary and gastrointestinal systems, in addition to the skin.[20] SJS was described in 1922 by 2 American physicians Albert Mason Stevens and Frank Chambliss Johnson and TEN in 1956 by Alen Lyell.[21,22,23] Though it has been decades since their discovery, still the categorization of SJS and TEN are a topic of ongoing controversy as clear knowledge is lacking on the etiopathogenesis and is still under redefinitions and reclassifications. EMF, SJS & TEN were considered a continuum of spectrum since 1983.[24] Later, it is redesignated by Bastuji-Garin et al in 1993 and Roujeau et al in 1994 and EMF is kept separately as it is predominately due to viral infections and is characterised by typical target lesions in acral areas.[25,26] In contrast, SJS and TEN once considered a distinct entity, were gradually considered one continuum of spectrum , as they are mainly due to drugs, differing only by the body surface area affected. Although some still believes that SJS and TEN are etiologically and pathologically distinct entities.[27]

50% of SJS is attributed to drug and the remaining to infection. 95% of TEN is attributed to drugs. Drugs are the predominantly noxious stimuli provoking this SJS-TEN spectrum of illness. Several drugs are at increased risk of causing SJS-TEN, including sulfonamide antibiotics, aminopenicillin, cephalosporins, quinolones, aromatic anticonvulsants, NSAIDS of Oxicam group. However recently, infection with Mycoplasma pneumonia, Klebsiella pneumonia, Herpes virus infection, Vaccination and Graft vs Host Disease(GVHD) have also been well documented to be causally associated.[28]

Certain diseases have known to increase the susceptibility of occurrence of these adverse drug reactions, examples are collagen vascular diseases, HIV infection, carcinoma, rheumatological disorder, autoimmune disorder and radiotherapy.[29,30] Genetic susceptibility have also been encountered in the occurrence SJS and TEN.[31]

The illness begins with flu like prodrome of cough, malaise, fever, running nose, arthralgia, myalgia and decreased appetite. Skin lesions begin as painful erythematous macules which evolve into blisters and the affected epidermis soon peels off. The epidermal detachment and mucous membrane erosions are due to sudden epidermal apoptosis. The diagnosis relies mainly on the clinical features along with the histopathological examination of skin biopsy, which shows full thickness epidermal necrolysis due to extensive keratinocyte apoptosis.[28]

Acute complications include fluid and electrolyte imbalance, secondary infection and septicemia, corneal ulceration, panophthalmitis, anterior uveitis, synechiae and blindness, gastrointestinal complications like oesophageal stricture, gastro intestinal erosion and colonic perforation can also occur. Proximal renal tubular damage and respiratory failure are few of life threatening complications. Loss of epidermis in the acute phase makes the patient vulnerable to infections and can result in sepsis, the leading cause of death in SJS-TEN spectrum of illnesses. Those who survive the acute phase suffer long term complications mainly of skin and eye, like scarring, pigmentary changes, eruptive melanocytic nevi, and dry eyes, respectively. Other chronic complications include oesophageal stricture, phimosis, urethral and anal stricture, vulvovaginal atrophy and permanent onychia.

Early initiation of supportive and definitive therapy and careful monitoring of patient, with early hospitalization helps decreasing the mortality. The various modality of treatment includes systemic corticosteroids, intravenous immunoglobulins, cyclosporine A and plasmapheresis. The therapeutic value of each is still controversial and conflicting.

Although rare, SJS and TEN have a significant impact on public health due to its high mortality. Mortality rate ranges from 1-5% in SJS to 10-15% in transitional forms and 25-35% in established TEN.[17,25,32,33,34] Various scoring systems had been employed for TEN including SAPS and Burn Scoring System,

which later proved to be non specific for SJS and TEN. So was formulated a specific scoring system for TEN, the SCORTEN.

SCORTEN is an illness severity score, developed and validated to predict the mortality in patients of SJS, SJS-TEN & TEN by Bastuji-Garin et al in the year 2000.[25]

CASE DEFINITION

SJS – epidermal detachment involving less than 10% body surface area plus widespread erythematous or purpuric macules or flat atypical target lesions and the involvement of 2 or more mucosa

SJS-TEN – epidermal detachment between 10% and 29% with widespread erythematous or purupuric macules or atypical target like lesions

TEN with spots – epidermal detachment more than 30% with widespread erythematous or purupuric macules or atypical target like lesions

TEN without spots – detachment in large epidermal sheets involving >30% BSA without purpuric macules and target lesions.

This widely accepted classification is proposed by Bastuji-Garin et al in 1993 and is still the most accepted one.[30]

INCIDENCE

The worldwide estimated incidence of TEN is 0.4 to 1.9 per million people and that of SJS is 1.2 to 6 per million people.[6,7,8,9] The estimated combined incidence of SJS/TEN overlap is 2 to 7 per million per year.[10,11,12,32] The incidence of TEN and SJS in Germany is 0.93 and 1.1 cases per million per year respectively.[33]An incidence of 1.2 cases per million per year has been recorded in France.[32] A study in India has reported the occurrence of TEN in 0.034% of 87514 dermatological outpatients.[16]

The incidence of SJS and TEN is 1000 fold higher in HIV infected individuals than in general population with an estimated incidence of 1 in 1000.[35]

AGE

SJS – TEN can occur at any age right from infancy through childhood, adolescence and adult, increased incidence is seen with increasing age.[28,32,33,36]

SEX

Females are affected slightly higher than males, with female: male being 1.5:1.[32,33,36] In various studies the male to female ratio ranges from 3:2 to 2:1.[37,38]

ETIOLOGY

Drugs have been identified as the most important etiological factors in 95% of TEN and 50% of SJS cases. 90% of cases show positive history of drug exposure prior to the onset.[3] Although any drug can cause SJS and TEN, NSAIDS, anticonvulsants and antibiotics are the most commonly implicated.

In India, anticonvulsants are the most common culprits for SJS and TEN, with phenytoin topping the list in a study by Sharma et al and Carbamazepine was found to be the most common offending agent in a study by Devi et al. Barbiturates, sodium valproate and lamotrigine have also shown positive association.[17,18]

Case reports of SJS and TEN occurring after the use of all the NSAIDS exists. Such are oxicam derivatives, ibuprofen, fenbufen, diclofenac, salicycylates, selective COX 2 inhibitors with special mention to pyrazolone derivatives and acetaminophenon in certain studies.[39, 40,41,42,43]

Among the antibiotics, sulfonamides deserve a special mention, especially long acting sulfonamides and cotrimoxazole.[33, 34, 44] The other offending drugs are beta lactam antibiotics, flouroquinolones, tertracyclines, vancomycin and antitubercular agents like isoniazid, thiacetazone and streptomycin.[45, 46,47,48,49] In an Indian study

by Kaur et al, ATT were reported to be the offending agent in 30% of patients.[16] There are reports of TEN from intranasal mupirocin.[50]

HIV patients on ART has reported an increased incidence of SJS and TEN earlier, due to Nevirapine in the first line drug regimen.[51, 52] And the drug has now been withdrawn from the first line of ART, thus decreasing the morbidity from this acute severe drug reaction.

There are also case reports of TEN after over-the-counter (OTC) eye drops [51-55] and OTC oral pseudoephedrine.[53]

DRUGS MOST COMMONLY ATTRIBUTED IN SJS and TEN

DRUG CLASS	ASSOCIATED DRUGS
Anticonvulsants	Carbamazepine, phenytoin, barbiturates, lamotrigine, felbamate
NSAID	Piroxicam, diclofenac, sulindac, ibuprofen, ketoprofen, naproxen, valdecoxib, celecoxib, rofecoxib
Sulphonamide	Co-trimoxazole, sulfasalazine, sulfadoxine, sulfadiazine
Antibiotics	Cephalosporins, flouroquinolones, vancomycin, aminopenicillins, doxycycline, erythromycin, ciprofloxacin
Antiviral	Nevirapine, Abacavir
Uric acid lowering	Allopurinol
Anti tubercular drug	Thiacetazone, rifampicin, isoniazid, ethambutol

Other less common drugs include antifungals like griseofulvin, terbenafine and fluconazole, antiulcer drugs like omeprazole, ranitidine and famotidine, antimalarials like hydroxychloroquine.[54-63] Cases have also been reported with Dapsone, Calcium channel blockers, thalidomide, methotrexate, TNF alpha blockers and gold.[64, 65]

MEDICATION CROSS-REACTIVITY:

Cross-reactivity between medications can occur between different beta-lactam antibiotics, such as penicillins and cephalosporins and among the antiepileptic agents, all aromatic compounds like carbamazepine, phenytoin and Phenobarbital show cross-reactivity.[66] However, a reaction to a sulfonamide antibiotic does not imply sensitivity to non-antibiotic sulfonamide drugs like thiazide diuretics or COX-2 inhibitors.[67,68]

OTHER ETIOLOGY:

Mycoplasma pneumonia infection, klebsiella pneumonia, herpes simplex virus, cytomegalovirus and dengue virus infections are the next common attributed cause to drugs in causing SJS/TEN.[69, 70, 71] Cases of TEN have been reported after vaccination like measles mumps rubella vaccination and after administration of contrast agents and after exposure to industrial chemicals and fumes.[72-77] It has also occurred in patients consuming natural remedies and traditional Chinese herbs.

ASSESSING THE DRUG CAUSALITY

Sassolas et al developed an algorithm of drug causality for epidermal necrolysis and reassessed the risk-benefit profiles of all cases enrolled in the EuroSCAR study. ALDEN (Algorithm of Drug causality in Epidermal Necrolysis) is used as a tool for the retrospective assessment of drug causality. It assigned each drug a score from -1 to 10 based on 6 parameters

1. Time delay from the initial drug intake to the onset of reaction
2. The probability of drug presence in the body on the index day
3. A previous history of adverse drug reaction to the same drug
4. The presence of the drug beyond the progression phase of the disease
5. The drug notoriety based on previous results of the SCAR study
6. The presence or absence of other etiologic causes

The score is categorized as very probable (>_6), probable (4-5), possible (2-3), unlikely (0-1) and very unlikely (<0).[78]

The causality of the drug can also be determined by the French Surveillance system.[32] According to this method, the drug is

1) **Highly suggestive** if the eruption began 7 to 21 days after first administration of drug or the eruption began within 48 hours of

administration if the drug had previously caused a similar reaction in the patient.

2) **Incompatible** if the drug had been administered after the disease onset or the eruption began within 24 hours of first administration of drug or the eruption began more than 21 days after withdrawal of drug
3) **Compatible** in all other cases.

RISK FACTORS FOR DEVELOPMENT OF SJS and TEN

- Age – elderly
- Pharmacokinetics – slow acetylator group
- Immunosuppression – Lymphoma, HIV infection[35]
- Concomitant administration of radiotherapy with anticonvulsants (expecially in those with brain tumor)
- **Genetics** : People of certain ethnic groups with certain human leukocyte antigen(HLA) subtypes have an increased incidence of SJS/TEN when exposed to specific drugs.[31]
    - HLA B*1502 – in Asian and East Indians, Hans Chinese decent and Indians exposed to carbamazepine.[79,80]
    - HLA A*3101 – in Europeans exposed to carbamazepine[81]

- HLA B*5701 and HLA B*5801– confers increased risk of Abacavir and Allopurinol induced hypersensitivity reaction respectively.[82-84]
- Polymorphism in TLR3 and EP3 – strong association with SJS in Japanese population.
- IFN gamma gene polymorphism – associated with SJS in Mexican population.[85]

- Family members of SJS/TEN may be susceptible to the same drugs.

PATHOGENESIS

Upon the intake of the implicated drug in genetically predisposed individuals' death of keratinocytes occur by the following mechanisms:

1) The pathogenesis is initiated by either non covalent direct interaction of drug antigenic moiety with MHC class I allotype or by covalent binding of a drug metabolite to a cellular peptide to form an immunogenic molecule.[86]
2) Later, T cell activation occur which causes keratinocyte death by soluble Fas ligand, perforin/granzyme/ TNF alfa and nitric oxide. Of these granulysin is suggested as the pivotal mediator of keratinocyte death .[87,88]
3) Fas – Fas L mediated apoptosis : drug interacts and causes upregulation of FasL by keratinocytes which constitutively express Fas , inducing apoptosis.[89,90]

4) The drug binds with MHC Class I expressing cells and induces them, resulting in secretion of Cytotoxic T cells within the epidermal blister, which kills the keratinocytes through perforin and granzyme.[91]
5) The drug activates NK cells and NK T cells and trigger cell death through granulysin and this doesn't require cell contact.[92]

In general, SJS/TEN is a T-cell mediated type IV hypersensitivity disorder and it can be considered an "immunologic burn". In the early stages, CD8+ T cells concentrate in blister fluid and epidermis, while CD4+ T cells in dermal layers. Later as the disease progresses, activated monocytes increases. Furthermore, soluble IL 2 receptor, a marker of activated T cells, is present in high level in blister fluid and serum and it correlates with the disease activity.[93]

Also, the level of cutaneous lymphocyte antigen (CLA), a skin-homing receptor, in the peripheral blood of TEN patients, correlates with the disease activity.[94]

CLINICAL FEATURES

The initial symptoms include prodrome of fever, upper respiratory tract symptoms and conjunctivitis mimicking febrile illness of infective origin. This is followed by mucous membrane detachment, followed by cutaneous lesions after 1-3 days.[37]

CUTANEOUS LESIONS:

The skin lesions first appear on trunk later spreads to neck & face and proximal extremities over a period of hours to 2-3 days. Morphology of skin lesions initially begin as erythematous, dusky red or purpuric macules of irregular shape and size with a tendency to coalesce with each other. Atypical target like lesion with 2 zones are also present. At this stage spontaneous Nikolsky is usually not present, but Nikolsky is positive on elicitation. This is associated with pain and burning sensation. Perilesional erythema is a sign of disease activity and helps to monitor treatment response. Later due to epidermal necrosis, fluid collects between epidermis and dermis leading to the formation of vesicle and bulla, which ultimately results in peeling of epidermis from dermis. Nikolsky sign can be elicited at the stage of blistering skin lesions. In some patients the initial presentation is in itself, extensive sheets of necrotic epidermis, with sheets of exfoliation i.e. with positive spontaneous Nikolsky sign. Atypical target like macules and annular patches are also scattered among other lesions.[28]

MUCOSA

Mucosal lesions manifests by pain in swallowing, photophobia, diarrhea, bleeding per rectum and painful micturition. Oral, Genital & Ocular mucosa is involved in more than 90% of patients. Mucosal lesions usually precede the skin

lesion by 3 days.[36,37] Extensive erosion of the buccal, palatal mucosa with hemorrhagic crusting of lips is common. Eye lesions ranges from catarrhal or purulent conjunctivitis to severe palpebral and bulbar conjunctival erosions and corneal erosions, which later lead to symblepharon and ankyloblepharon formation. Urogenital system involovement manifests by erosion of scrotum, balanoposthitis and phimosis in male and vulval erosions in female with symptoms of acute urinary retention in both.

Necrolysis of bronchial epidermis has been demonstrated to occur in 25% of cases. In respiratory system, signs are greater than the symptoms, with CXR changes being important.[95] Rare symptoms include gastrointestinal manifestations like diarrhea and still rarer are paronychia and acute shedding of nails.

FIRST EPISODE

The usual interval between the onset of drug intake and SJS – TEN is between 7 and 21 days. This period is required for sensitization.

RECURRENT EPISODE

In case of re-exposure symptoms appear within 2 days, due to memory of the immune system.

RECOVERY:

Re-epithelialisation usually starts within few days of cessation of disease activity and is completed by about 3 weeks except mucosa and pressure sites which takes longer. [96]

DIAGNOSIS

Diagnosis is primarily based on the characteristic clinical findings and history.[97,28] Early Toxic Epidermal Necrolysis resembles morbilliform eruption and it need to be differentiated from more benign drug reactions like erythema multiforme major and exanthematous drug reactions. Epidermal necrosis seen in histopathology has high sensitivity and low specificity for diagnosing TEN. Patch testing in SJS/TEN to test for susceptibility to a specific drug has been attempted, but the results have been disappointing. Newer experimental diagnostic tools like serum granulysin and high mobility group protein B1 (HMGB1) can differentiate TEN from non specific drug reactions. But these tests are not validated yet and are not readily available now.[98,99] An invitro lymphocyte toxicity assay to measure activity of detoxification enzymes exists but only as a research tool.[100]

HISTOPATHOLOGY

Early lesions show a moderate perivascular mononuclear infiltrate in the papillary dermis, with epidermal spongiosis and exocytosis. Satellite cell necrosis

i.e. close apposition between mononuclear cells and necrotic keratinocytes may be seen.

In fully established lesions, there is full-thickness necrosis of the whole epidermis, with sub epidermal blister formation and mononuclear inflammatory infiltrate.

Comparative studies on the biopsy specimens of patients with EM and SJS-TEN have demonstrated distinct histological patterns in both the diseases.[101] In EM, there is less of epidermal necrosis, more dermal inflammation and more exocytosis. Conversely, in SJS-TEN, there is moe epidermal necrosis, less dermal inflammation and also less exocytosis as compared to EM. These findings further support the difference observed in the clinical patterns and pathogenetic mechanisms of the two disorders.

A study by Quinn et al has also uncovered the prognostic significance of histological findings in patients with TEN.[102] The biopsy specimens of 37 patients were studied for the degree of dermal inflammation and mean number of mononuclear cells. It was found that while 73% of patients with sparse inflammation survived, only 47% with moderate and 29% with extensive inflammation survived. The accuracy in predicting outcome was 65% using grade of inflammation and 68% with the mean cell count.

IMMUNOFLORESCENCE TEST

In a study by Maciejewska et al, DIF showed no immune complex deposition in epidermis or in the dermal-epidermal junction and IIF was negative. Similar observation was made by harr et al and Roujeau et al.[103-105]

DIFFERENTIAL DIAGNOSIS

Staphylococcal scalded skin syndrome, Generalised Fixed drug eruption, acute lupus erythematosus, acute severe GVHD, erythema multiforme, drug induced linear IgA bullous dermatoses, Toxic erythema of chemotheraphy, acute generalized exanthematous pustulosis and rarely pemphigus vulgaris and bullous pemphigoid are some of the differential diagnosis.[28]

LABORATORY ANOMALIES

Laboratory parameters derangement is useful in the assessment of prognosis. Abnormal Blood Urea, Serum bicarbonate and blood sugar values are individual parameters associated with statistically significant poor prognosis.[5] Other hematological abnormalities noted are anaemia, thrombocytopenia, leukocytosis or leukocytopenia.[37,106] Slight increase in aminotransferases occurs in around 50% of cases. Subclinical Interstitial infiltrate in chest x ray is a common early finding.[95]

COMPLICATIONS

ACUTE COMPLICATIONS

Most of the acute complications occurs as a result of extensive epidermal necrolysis and are proportionate to the extent of epidermal detachment. The total daily fluid loss is 3-4 litres in adult patients with epidermal detachment of 50% body surface area. Electrolyte, fluid and protein loss results in reduction of intravascular volume. Consequently, blood flow to the kidney decreases and pre-renal azotemia sets in. This results in elevation of blood urea nitrogen and creatinine with decreased urine output. If hypovolemia is not corrected in this stage, pre-renal acute kidney injury occurs.[3]

Necrotic epidermis and exudates support the growth of wide range of micro-organisms despite barrier nursing. Staphylococcus aureus commonly colonises the skin in the first few days.[16] Later, gram-negative rods like Pseudomonas aeruginosa invades.[36, 107] Central venous lines and catheters carry a high risk of promoting systemic infection. Septicemia ensues causing multi-organ failure and appreciable mortality. Septicemia usually occurs as a result of Staphylococcus aureus or Pseudomonas aeruginosa.

Usually patients have shivering and fever, however, hypothermia may also occur in the setting of severe infection and irreversible septic shock.

The metabolic response to widespread skin lesions is extensive and resembles that of burns patients. Energy expenditure increases to twice the basal metabolic rate, when 50% or more of the body surface area is involved. Protein loss may increase to 150-200 grams per day. Inhibition of insulin secretion and/or insulin resistance in peripheral tissues is frequent, resulting in elevated plasma glucose levels and sometimes overt glycosuria.

Pneumonia or pneumonitis, due to sloughing of the tracheobronchial occurs in upto 30% of the cases. Hyperventilation with mild hypoxemia is usual due to metabolic acidosis. Subclinical interstitial edema is noticed in the early X-ray films. Adult respiratory distress syndrome (ARDS) can occur which is the leading cause of death in TEN in few of the studies.[95]

Conjunctival and corneal erosions with symblepharon (partial or complete adhesion of the palpebral conjunctiva of the eyelid to the bulbar conjunctiva) and ankyloblepharon (partial or complete fusion of eyelids by webs of skin) formation can occur during acute episode of SJS/TEN.

Disseminated mucosal erosions have occasionally been reported to occur in the gastrointestinal tract. The malphigian epithelium of the oesophagus is the most commonly involved, leading to dysphagia and sometimes bleeding. Overt intestinal symptoms are uncommon and may manifest as non-specific bloody diarrhea.

CHRONIC COMPLICATIONS AND SEQUELAE

- Scarring occurs at pressure sites and at areas where secondary infections occurred initially.
- Dyspigmentation – both hyperpigmentation and hypopigmentation[7]
- Eruptive melanocytic nevi – especially in children and young adults
- Nail dystrophy, onycholysis
- Diffuse hair loss
- Pruritus
- Persistent mucosal erosion
- Ocular sequelae is the most common, described in 20-79% of patients. This includes dry eye syndrome, symblepharon, corneal scarring, corneal neovascularization, corneal xerosis, trichiasis, reduced visual acuity, blindness and subconjunctival fibrosis. Dry eye syndrome (chronic loss of sufficient moisture in the surface of the eye characterized by irritation and easily fatigued eye) is the most common ocular sequelae and it may occur even in those who did not experience acute ocular involvement. Patients expressing HLA DQ B1*0601 allele has an increased risk of Ocular complications.[108]

- Dental sequelae include oral discomfort, reduced mean saliva flow, increased saliva acidity, periodontal disease, gingival inflammation and synechiae formation.[109]
- Genitourinary complications include dyspareunia, adhesions and introital stenosis in women and erosive balanitis, urethral erosions and phimosis in men.
- Pulmonary complications include decrease in DLCO (diffusion capacity of lung for carbon monoxide) for one to one and half years after discharge. Chronic sequelae include chronic bronchitis, bronchiectasis, bronchiolitis obliterans, organizing pneumonitis and respiratory tract obstruction.[3,110]
- Significant psychological problems occur on the survivors and the immediate family members.

MANAGEMENT OF ACUTE EPISODE

Management includes early recognition of the condition, prompt withdrawal of the suspected drug(s) if any, admission, appropriate supportive therapy, initiation of specific therapy, management of complications and prevention of sequelae and prevention of recurrences.

Multidisciplinary approach is helpful in the management of these patients owing to the systemic nature of the disease. Surgical intervention is rarely necessary in SJS/TEN.[3]

WITHDRAWAL OF THE OFFENDING DRUG:

Stopping the implicated drug is of extreme importance as this would abort the process of acute skin failure and re-epithelization will ensue in a shorter period of time.[112] However, in drugs with long t1/2, the reaction continues for quite sometimes after the cessation of drug due to accumulation of drug or its toxic metabolites. In case of single drug intake it is easy to identify and stop the drug, but in polypharmacy stop all the drug or restrict it to the minimum possible by giving only the absolutely life saving ones. Substitution is usually made with structurally unrelated drug to the implicated one.

SUPPORTIVE THERAPY:

Environmental temperature should be maintained at 30-32 ºC to prevent the calorie loss through the skin. Hot air-warmer can be used for this purpose. Adequate and aggressive fluid and electrolyte management is the mainstay of therapy in the first few days. Parkland formula, widely used in fluid calculation in burns patient holds good for TEN patients, with 3/4th of the volume being enough. Parkland formula is 4ml/kg body weight/% BSA involved. Adult patient with 50%

BSA involvement loses 3-4 L of fluid every day. Half the calculated fluid is administered in the first 8 hours and the other half in the next 16 hours. After 24 hours, fluid requirement is based on intake/output status of the patient, so as to maintain the urine output between 1000 to 1500ml.[113]

Fluid loss is accompanied by loss of electrolytes like sodium, potassium, chloride and phosphate. Hypophosphataemia in these patients aggravates the insulin resistence. Careful replacement of electrolytes, according to the serum electrolyte levels should be done. The choice of fluid is ringer lactate or normal saline.

If adequate nutrition is not given, dehydration sets in, urine becomes hyperosmolar, urine output decreases and slowly blood urea and creatinine increases and pre-renal azotemia sets in. Overcorrection leads to pulmonary edema.

Sheriden and colleagues reported no deaths in 10 children with TEN treated with supportive care alone.[114] In another study, 21 children with SJS/TEN were treated with conservative measures alone, and none died.[115] In another, 15 children with SJS/TEN treated in a Burn ICU with supportive care alone reported a mortality of 7%.[116]

ENTERAL NUTRITION

Gradual changing over from parentral nutrition to oral fluids should be done. Early introduction of enteral nutrition decreases the incidence of stress ulcers, stasis syndrome and bowel infection.

Once patient establishes enteral feed, care should be provided to take adequate proteins and micronutrients. During the early recovery phase 2-3 times the average daily requirement of protein is needed. The calculated calorie requirement is 30-35kcal/kg/day and protein is 1.5-2g/kg/day to prevent negative nitrogen balance.

SKIN CARE:

Leave the detached epidermis in place, so it provides a natural dressing. Regular cleaning of the denuded area with normal saline reduces the chance of secondary infection. Gentian violet paint and 0.5% silver nitrate is useful for the denuded area, especially flexures. Silver sulfadiazine is avoided in SJS/TEN as sulfonamides are frequently implicated in SJS/TEN.

Dressing of the denuded area is to be done with paraffin or petrolatum gauze, with or without antibiotic impregnation. Adhesive dressing should be avoided. Frequent change of posture and water bed helps in preventing the occurrence of pressure sores. The importance of skin care in SJS/TEN cannot be

emphasized enough, as this if instituted properly prevents sepsis and mortality in SJS/TEN.

OCULAR MANAGEMENT

Use of lubricant and topical eye drops every 2nd hourly is practiced routinely. Synechiae developed should be disrupted with a blunt instrument. Amniotic membrane transplantation and gas permeable scleral contact lens therapy can be used for patients with severe corneal and conjunctival involvement.[73,83,108]

RESPIRATORY MANAGEMENT

Careful monitoring of respiratory function should be done. Nasal supplemental oxygen is given if necessary. Bronchial aspiration, bronchodilators and saline nebulization are also of use. Prompt intubation and mechanical ventilation if trachea and bronchi are involved.[14, 110]

ORAL CAVITY CARE

Frequent saline goggling, antiseptic spraying and anaesthetic mouth washes are used to maintain oral hygiene. Saline compresses followed by lubricant application helps in the removal of crusts in lip.

PSYCHOLOGICAL SUPPORT:

Providing emotional support and maintaining conversation with the patient is a vital part in supportive care and this addresses the patients fear and anxieties and lets us educate the patient about self care and prevention of further episodes.[111]

DEFINITIVE THERAPY:

There is no definitive standard guidelines for the management of SJS and TEN till date.

Prompt withdrawal of the offending drug decreases the mortality by 30% per day as estimated by Garcia et al.

Numerous immunomodulatory drugs have been tried by many with conflicting results, such as corticosteroids, cyclosporin, intravenous immunoglobulin, cyclophosphamide, plasmapheresis and tumor necrosis factor α inhibitors.[3,113]

Corticosteroids have been in use since the early days of literature and are still under conflict. It is proposed as the management as this severe drug reaction is believed to be a hypersensitivity reaction. Corticosteroids are used in the form of intravenous dexamethasone or methylprednisolone in early stages. A study by Halebian et al in America has shown that mortality of TEN fell from 66% to 33%

upon corticosteroid usage.[117] Another retrospective study by schneck et al had showed no significant difference in corticosteroid vs supportive therapy group.[118]

Intravenous Immunoglobulin: On the basis that Fas- FasL interaction is an important pathology of SJS and TEN, IvIg are tried as blocking antibodies. The usual dose is 2 g/kg administered over 2-4 days. A large retrospective study by Prince et al showed that IvIg has rapidly arrested the progression of epithelial necrosis and favoured early recovery. However another study by Schneck did not show any significant difference in morbidity and mortality when compared with supportive therapy alone.[118, 119,120]

Plasmapharesis acts by removing the toxic metabolites or antibodies from the blood. A study by Egan et al has shown zero mortality in 6 patients treated with plasmapheresis. However no other large scale studies are available to support this.[13]

Other drugs tried are cyclosporine in the dose of 3-5mg/kg, N acetyl cysteine, thalidomide and pentoxiphylline. However, only case series and case reports are available for these.[121-123]

PROGNOSIS & OUTCOME

The overall prognosis depends on the stage at which the treatment is initiated, age of the patient, extent of necrolysis, associated comorbidities and

accompanying complications (electrolyte imbalance, adult respiratory distress syndrome, sepsis, hepatic and renal impairment).The mortality rate of SJS ranges from 1-5% and that of TEN is 25-35%.[124] Sepsis leading to multi-organ failure is the leading cause of death with additional morbidity from gastrointestinal bleeding, pulmonary embolism, myocardial infarction and pulmonary edema.

A number of factors are associated with poor prognosis and such individual risk factors include continuing the offending agent, long half life of the drug, delayed hospitalisation, advanced age, elevated blood urea, creatinine, blood sugar, low serum bicarbonate, anaemia and thrombocytopenia. Since there are many parameters, a constellation of significantly associated parameters are made and scoring system is created.

SCORING SYSTEM

- **SAPS II** – Simplified acute physiology Score II – based on 15 weighed variables. This score is currently in use in ICU to estimate the probability of hospital mortality.
- **Burn Scoring System** – (age + percentage of BSA involved on admission)
- **SCORTEN:** SCORTEN (SCORe of TEN) model is a logistic regression equation that can be used to translate the score into a probability of mortality.[5] It is intended to be completed within 24 hours of admission and

again of day 3 of hospitalization.[7] It represents the number of abnormal parameters among the seven independent prognosic factors with a weight of 1 assigned to each .

- Age > 40 years
- Heart rate > 120 beats per minute
- Comorbid malignancy
- Epidermal detachment on Day 1 >10% BSA (summation of detached and detachable epidermis)
- Blood urea nitrogen >28mg/dl
- Glucose >252 mg/dl
- Bicarbonate <20mEq/l

Independent factors related to poor outcome despite that in SCORTEN are elevated creatinine, neutropenia, lymphopenia and thrombocytopenia.

Previous three prognostic factors –age, BSA and blood urea nitrogen levels were highlighted by Revuz et al, latter TEN associated bronchial epithelial necrosis has been prospectively demonstrated as the major cause of death by Lebargy et al in 1997 and recently, Garcia-Doval et al have observed that prompt withdrawal of the culprit drug decreases the mortality.[36,110,112]

Other clinical parameters reported previously to be predictive of mortality include thrombocytopenia, leucopenia, and delay in hospital admission.[6, 125-127]

PREVENTION

The Human Leukocyte Antigen genotype testing, aids in preventing the administration of drugs to susceptible individuals, thus reducing the incidence of this deadly condition.[80,81]

STEPS TO PREVENT RECURRENCE:

Health educating the patients and family members about the reaction to the particular drug and other cross reacting drugs should be done and issuing drug allergy alert cards will help.[67, 68]

DESENSITISATION:

In certain scenerios, it is important to give the offending drug to treat the primary condition, eg tuberculosis. In such case desensitization is important. The priniciple is to gradually increase the dose of drug on successive days until the full therapeutic benefit is reached. Kura et al, have conducted a studyon desensitisation for ATT, he was successful in 7 patients although one developed second episode of TEN with pyrazinamide. Thus, desensitization is a double edged sword as this can cause a potentially fatal drug reaction.[128]

FUTURE PROSPECTS:

Further modifications possible for improving research in this subject are

- Routine HLA genetic screening for predicting SJS and TEN
- Serum granulysin and HMBG1 for early and definitive diagnosis of TEN and SJS
- Correlation of SCORTEN with various treatment modalities
- Devising of a standard treatment protocol for TEN

MATERIALS AND METHODS

METHODOLOGY:

This prospective observational study was conducted in the Department of Dermatology, Venereology and Leprosy, Tirunelveli Medical College, Tirunelveli from January 2016 to June 2017 after obtaining Institutional ethical committee clearance. The study population consisted of all consecutive clinically diagnosed cases of Stevens Johnson syndrome and Toxic Epidermal Necrolysis and SJS-TEN overlap who fulfilled the inclusion criteria. Patients belonging to all ages and both sexes were included in the study. All patients were treated as inpatients in skin ward or Intensive Medical care Unit in Tirunelveli Medical College Hospital.

Both informed and written consent was obtained from all patients or from their guardians, as and when applicable to include them in the study and to carry out necessary investigations, and to take clinical photographs.

A thorough clinical history, including the demographic data of the patient, residence and occupation were recorded on a pre-designed questionnaire in their native language. Patients were enquired thoroughly for history of any prodromal symptoms, onset and duration of the illness and also about the site, distribution and progression of lesions. Past history of any previous similar episodes and history of significant medical illnesses like Diabetes, Hypertension, Tuberculosis, Chronic

liver or kidney disease was recorded. History of other possible etiologies like upper respiratory tract infections, viral hepatitis, urinary tract infections, herpes simplex infections, irradiation, vaccination and organ transplantation was also elicited.

History of drug intake 3 weeks prior to the onset of first clinical symptom of SJS and TEN was recorded.

A thorough general physical and systemic examination was carried out for all patients including recording of Blood pressure, pulse rate, respiratory rate, temperature and intake and output chart. A detailed mucocutaneous examination was conducted to evaluate the morphological pattern, site and extent of skin lesions, mucosal involvement and presence of skin tenderness. Nikolsky sign was elicited for all patients. The area of epidermal detachment was calculated according to the Wallace Rule of Nine.

Patients were photographed on the day of admission and subsequently during the hospital stay and during the follow up period.

All patients were followed up for the progression of skin lesions and the area of epidermal detachment.

All patients were classified into one of the 3 categories according to the Consensus classification proposed by Bastuji-Garin et al[25], which is as follows

1. SJS : epidermal detachment <10% body surface area
2. SJS-TEN OVERLAP: epidermal detachment of 10-30% body surface area
3. TEN: epidermal detachment >30% body surface area

Complete investigation of patients including complete hemogram, random blood sugar, liver and renal function tests, serum electrolytes and investigations needed for SCORTEN including bicarbonate level were done. Other investigations like serology for syphilis and HIV and chest X ray were carried out for all patients. Skin swab culture and sensitivity, throat swab, urine and blood culture and sensitivity were also done for all patients. Ultrasound of abdomen and pelvis, stool for occult blood and peripheral smear for atypical cells were done in all patients to rule out malignancy. Histopathological examination of skin lesions was also carried out for all patients.

SCORTEN analysis was done in all patients on day 1, 3 and 5. It is an illness severity score developed to predict the mortality in SJS and TEN. There are 7 parameters in SCORTEN, which are

1. Age above 40 years
2. Presence of malignancy
3. Tachycardia (heart rate above 120 beats per minute)
4. Initial percentage of epidermal detachment >10%

5. Blood urea nitrogen >28mg/dl
6. Serum glucose >252mg/d;
7. Bicarbonate level <20mmol/L

Each parameter is given a score of one and total score was calculated by summing up the number of abnormal parameters. The score was calculated for all patients on day 1, day 3 and day 5 of admission. The difference between SCORTEN values on day 1, 3 and day 5 of admission was evaluated by Kruskal Wallis test.

The mortality rate as predicted by SCORTEN values are as follows (Table 1)

SCORTEN	MORTALITY (%)
0-1	3.2
2	12.1
3	35.3
4	58.3
≥5	90.0

Table 1: SCORTEN and predicted mortality

The accuracy of SCORTEN for predicting mortality was assessed on day1, 3 and 5 of admission. The difference in SCORTEN between alive and dead patients was analysed by Mann-Whitney test. The individual parameters included in SCORTEN were tested by Fischers Exact Test.

All patients were put on conservative management in the form of withdrawal of suspected drug, fluid and electrolyte management, temperature regulation, barrier nursing and prophylactic antibiotics. IV corticosteroid was given to all patients and IvIg was given in one child case as an adjuvant to steroids. An interdisciplinary approach was followed, necessary ophthalmological consultation and medical opinion were obtained as and when required.

The patients were followed till complete recovery and the time taken for the healing of mucosal and skin lesions were recorded separately.

The patients were followed up and complications like pigmentary changes, scarring, contractures, dry eyes, conjunctivitis, ectropion/entropion, corneal scars, symblepharon, xerostomia, dysphagia, dyspareunia and urinary retention were noted.

INCLUSION CRITERIA

All clinically diagnosed cases of SJS, SJS-TEN Overlap and TEN

EXCLUSION CRITERIA

- Patient who came for admission after 1 week of onset of symptoms
- Patient who got treatment outside are excluded

STATISTICAL ANALYSIS AND INTERPRETATION

The study subjects had been described according to their type of variables. The variables which were continuous, were described in terms of means and categorical were described in terms of percentages. The significance of them were Interpreted by independent "t" and if more than two groups by ANOVA (Analysis of Variance) tests in respect of continuous variables. The significance of categorical variables was interpreted by χ^2 (Chi-square test). The Standardized Mortality Ratio was used to signify the predicted and observed mortalities of TEN subjects. The p-values ($p \leq 0.05$) less than or equal to 0.05 were treated as statistically significant.

OBSERVATIONS AND RESULTS

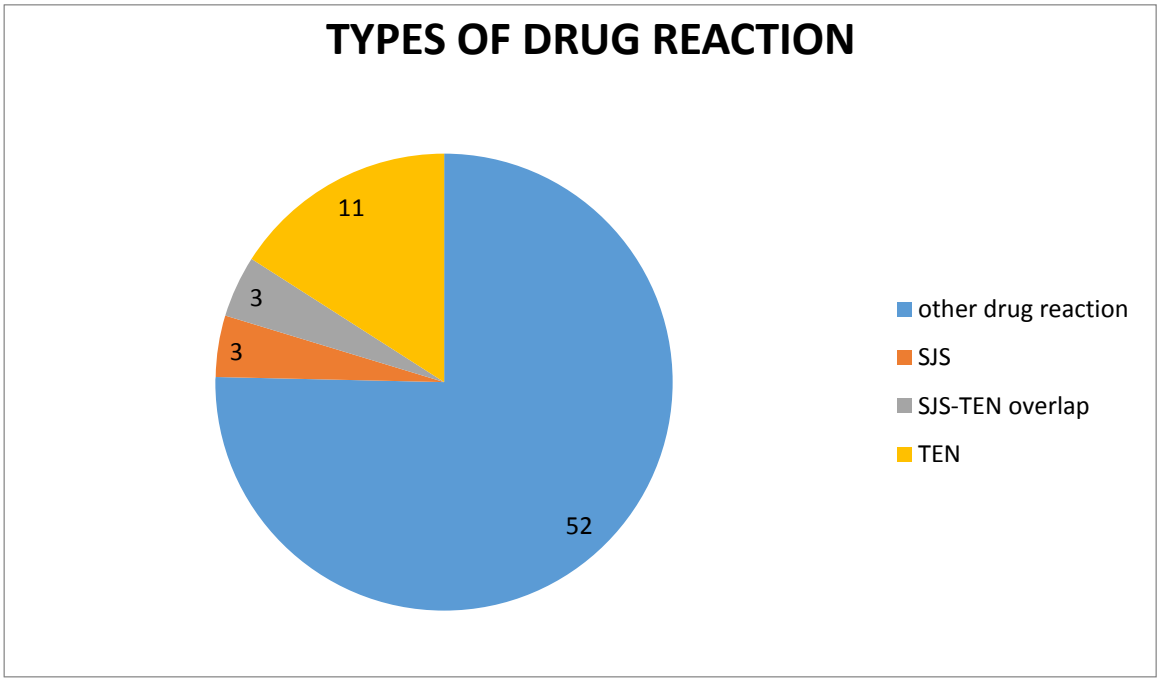

Figure 1: Types of drug reaction

Sixty nine cases of drug reactions were reported during the study period. Of these, 19 cases were in the SJS-TEN spectrum, including 3 SJS, 3 SJS-TEN overlap, and 13 cases of TEN. 2 cases of TEN were excluded from the study, as they were admitted 1 week after the onset of reaction.

So, 17 cases including 3 SJS, 3 SJS-TEN Overlap and 11 TEN formed the study population. Of this, 14 cases were first episode and 3 cases were 2nd episode including 2 cases of TEN (1 to T. Ibuprofen and another to T. Aspirin+Caffeine combination) and 1 case of SJS-TEN Overlap (to T. Phenytoin).

DEMOGRAPHIC PROFILE

Age group (years)	Male		Female		Total	
	Frequency	%	Frequency	%	Frequency	%
0-9	0	0	1	5.9	1	5.9
10-19	3	17.6	0	0.0	3	17.7
20-29	1	5.9	1	5.9	2	11.8
30-39	3	17.6	1	5.9	4	23.5
40-49	3	17.6	0	0.0	3	17.6
50-59	0	0	0	0.0	0	0.0
60-69	3	17.6	1	5.9	4	23.5
Total	13	76.4	4	23.6	17	100.0
Mean ± SD	39.2±18.4		35.5±24.7		38.1±19.3	
Sig.	"t" =0.417, df=15, p>0.05				Range=6-67 =61 yrs	

Table-2: Age and sex distribution of study subjects

The mean age of incidence among males was 39.2±18.4 years and the same for females was 35.5±24.7 years. The difference of age between the gender was not statistically significant (p>0.05). The mean age of incidence of total subjects was 38.1±19.3 years with range of 6 years to 67 years. Of the 17 cases, 13 were male and 4 were female including a male child (11 years) and a female child (6 years) respectively.

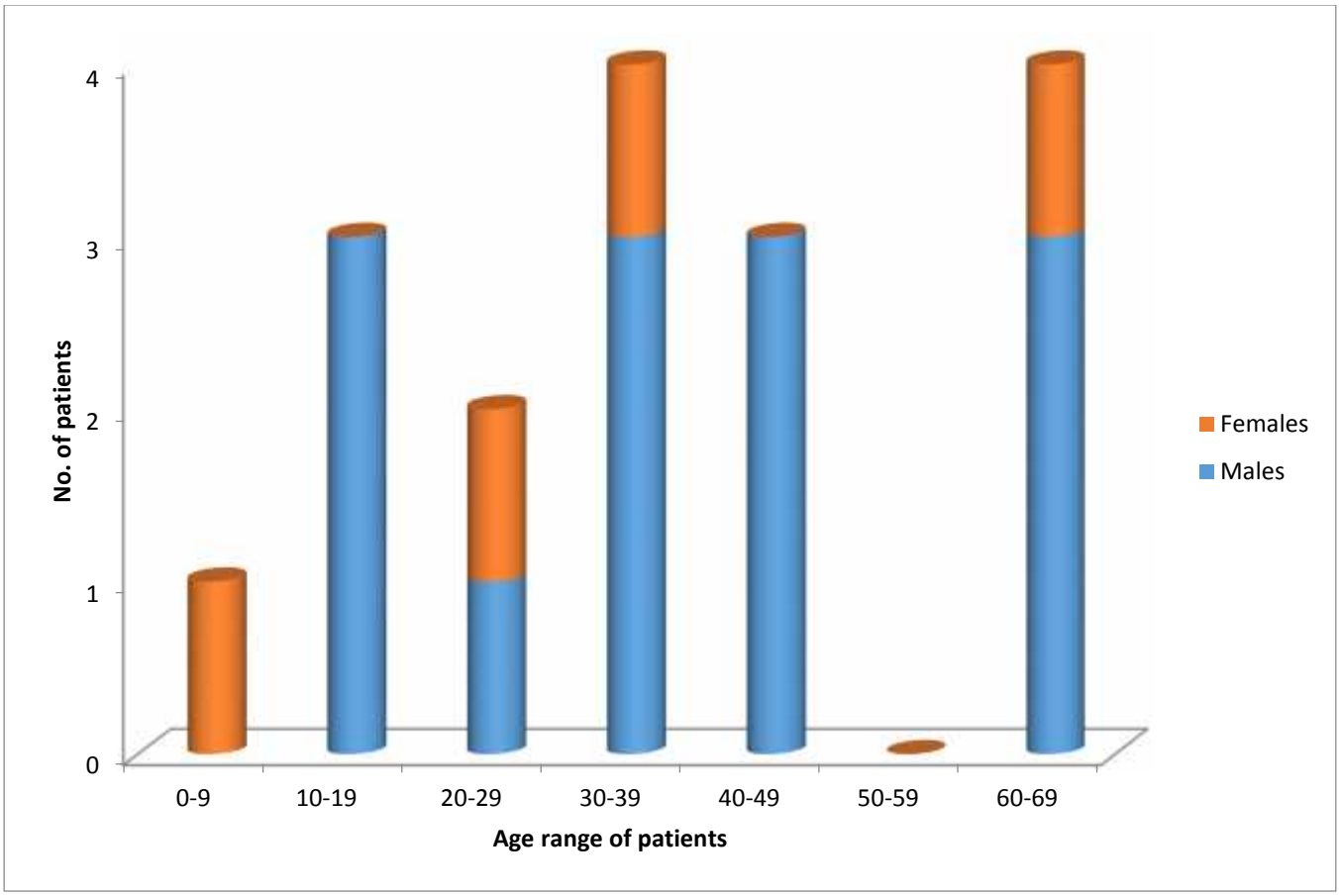

Figure 2: Age and sex distribution of study subjects

ONSET OF DISEASE:

Duration of onset:

The patients presented to the hospital within 3 days of the onset of cutaneous lesions (median 3 days, range 1 -6 days). Nearly half the patients, 8(47.05%) presented within 3 days of onset, while 2 of the patients presented on the day of onset itself, as it was the second episode in them.

Site of onset

The lesions began from the mucosa in 8(47%) cases, whereas in 7(41.7%) cases, the skin lesions were preceded by the mucosal lesions and in 2 cases (11.76%) simultaneous onset in skin and mucosa was observed. On the skin, trunk was the first site of onset in 12(70.58%) of the 17 patients, followed by face and neck in 3(17.64%) and proximal extremities in 2(11.76%). In mucous membrane, the oral mucosa was the first to be involved in 16 of 17(94.11%) patients, including 5(29.41%) patients with simultaneous onset of lesion in oral and genital and in 1(5.88%) patient genital was the first involved mucosa.

Prodromal symptoms

Majority of patients, 12(70.58%) gave a history of prodrome prior to the onset of cutaneous lesions. Fever with malaise was the most common systemic prodrome observed in the study, being present in 7(41.2%) of 17 patients. With the next common being conjunctivitis and URI in 3 patients (17.7%) and cough was present in 2(11.8%). Nine cases (52.94%) had cutaneous prodrome, with the common symptom being itch in 5(29.41%) followed by skin pain in 3(17.64%) and burning sensation in 2 (11.76%) patients. Of these, burning sensation was present in 2 cases (11.76%) of 2nd episode of TEN. All 3 cases who complained of skin pain were of TEN spectrum.

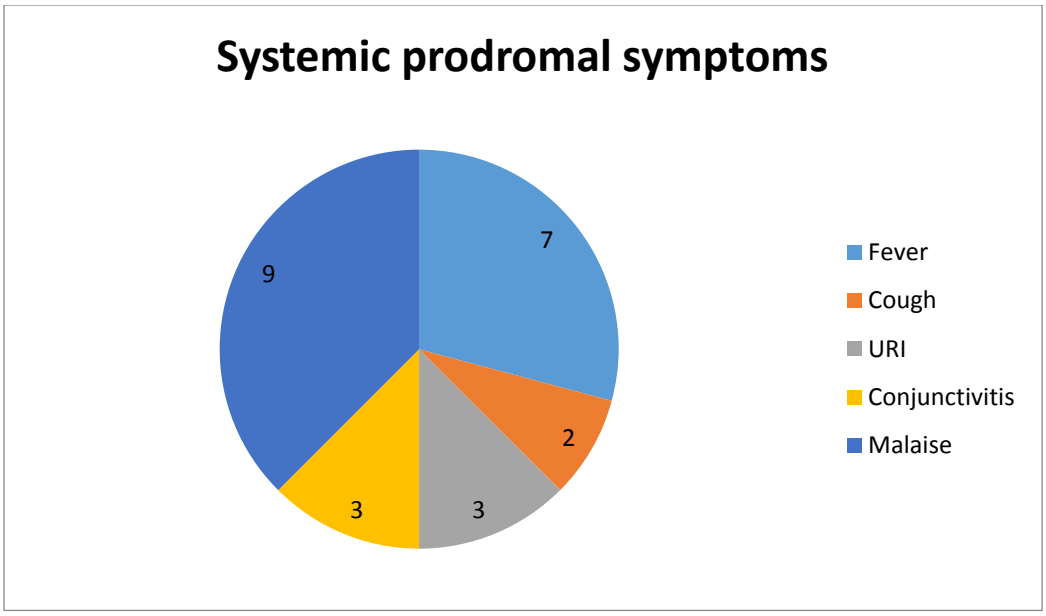

Figure 3: Systemic prodromal symptoms

PRODROME	Duration	SJS		SJS-TEN overlap		TEN	
		No	%	No	%	No	%
Itch	0	0	0.0	0	0.0	1	9.1
	12 hrs	0	0.0	0	0.0	1	9.1
	1 day	0	0.0	0	0.0	1	9.1
	5 days	0	0.0	1	33.3	0	0.0
	6 days	1	33.3	0	0.0	0	0.0
Skin Pain	1 day	0	0.0	0	0.0	2	18.2
	4 days	0	0.0	0	0.0	1	9.1
Burning sensation	30 minutes	0	0.0	0	0.0	2	18.2

Table-3: Classification of cutaneous PRODROME with duration according to diagnosis:

PAST HISTORY OF SIMILAR EPISODES:

3 patients had similar episodes in the past. 2 patients had to analgesics and one to phenytoin tablet. All three of them presented with toxic epidermal necrolysis in the first episode. Recurrence of reaction to analgesic occurred after a single dose, and cutaneous prodrome was prominent in both of them. Whereas to T.Phenytoin, the reaction occurred only after 40 days of drug intake and the severity was less than in the first episode. The same patient presented with TEN in first episode after 31 days of intake of T. Phenytoin and SJS in the second episode, which occurred only after 40 days of drug intake.

PRESENTING COMPLAINTS OF THE PATIENT

Complaints	SJS, n=3		SJS-TEN overlap, n =3		TEN, n=11		Total n=17	
	No	%	No	%	No	%	No	%
Red spots	0	0.0	2	66.7	4	36.4	6	35.3
Blistering	0	0.0	0	0.0	8	72.7	8	47.1
Skin pain	0	0.0	1	33.3	7	63.6	8	47.1
Painful oral lesions	3	100.0	3	100	11	100	7	41.2
Skin peeling	1	33.3	0	0.0	3	27.3	4	23.5
Black discolouration	0	0.0	1	33.3	3	27.3	4	23.5
Eye redness and pain	2	66.7	1	33.3	1	9.1	4	23.5
Lip and genital lesion	1	33.3	1	33.3	0	0.0	2	11.8

Table-4: Presenting complaints of the subjects:

The maximum complaints among the SJS subject was Painful oral lesions, which was present in all patients (100%). The SJS-TEN Overlap subjects, also had 100% oral mucosa involvement followed by purpuric spots in 2 (66.7%). The skin pain was experienced by 7 cases (63.6%) of TEN spectrums. Thus, among total subjects, painful oral lesion was present in all, followed by blistering and skin pain in 8(47%) patients.

Subjects	**Duration (Days)**		**"F"**	**Df**	**Significance**
	Mean	SD			
SJS	5.7	3.9	1.236	(2,14)	p>0.05
SJS- TEN Overlap	5.0	0.0			
TEN	3.5	2.3			
Total	4.1	2.4			

Table-5: Comparison of complaints duration between the three group subjects.

The table-5 compares the duration of complaints between the three groups. The mean duration between the three groups were not statistically significant (p>0.05).

The mean duration of complaints after which the patient presented to us was 5 days in SJS and SJS-TEN Overlap and 3 days in TEN.

CAUSATIVE DRUGS IMPLICATED

Of the 17 cases, history of drug intake was present in all (100%) and the causative drug was identified in 16 cases(94.11%) and 1(5.88%) was unidentified, which was due to analgesic. 8(47.05%) were due to anticonvulsants , 6(35.29%) to analgesics and 3(17.64%) to antibiotics. Individual drug wise, Phenytoin being the commonest cause leading to 5 cases (29.41%) in our study, next being carbamazepine in 3 cases (17.64%) followed by aceclofenac in 2 cases(11.76%) and others as mentioned in table 6.

CAUSATIVE DRUG		**NO OF CASES**			**TOTAL**
GROUP	**SUB GROUP**	**SJS**	**SJS-TEN Overlap**	**TEN**	
Anticonvulsants	T.Phenytoin	1	1	3	5
	T. Carbamazepine	0	1	2	3
Analgesics	T. Ibuprofen	0	0	1	1
	T. Aceclofenac	2	0	0	2
	T. Anacin (aspirin+caffeine)	0	0	1	1
	Paracetamol suppository	0	0	1	1
	Unidentified analgesic	0	0	1	1
Antibiotics	T. Norfloxacin	0	1	0	1
	Inj Ampicillin	0	0	1	1
ATT		0	0	1	1
	TOTAL	3	3	11	17

TABLE 6: List of causative agents

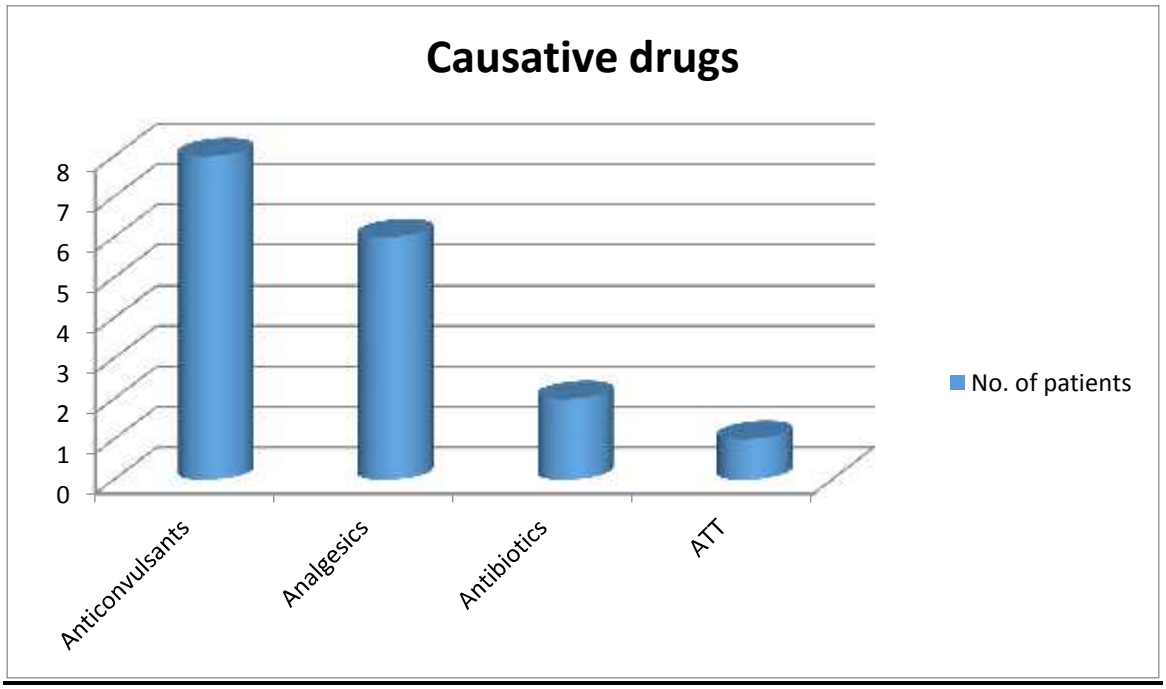

Figure 4: causative drug

WITHDRAWAL OF OFFENDING AGENT

There was no delay in withdrawal of offending agent in 6 cases (35.29%). The mean delay in stopping the drug after the onset of reaction is 3 days. This is due to delayed hospitalization in most of our cases, except 1 case, where a delay of 5 days was due to delay in recognition of etiological agent as it was rectal suppository of Paracetamol. Of the 3 cases who succumbed to death, there was no delay in stopping the inflicting drug in 2 cases and there was a delay of 3 days in 1 case, which again, was due to delayed hospitalization**.**

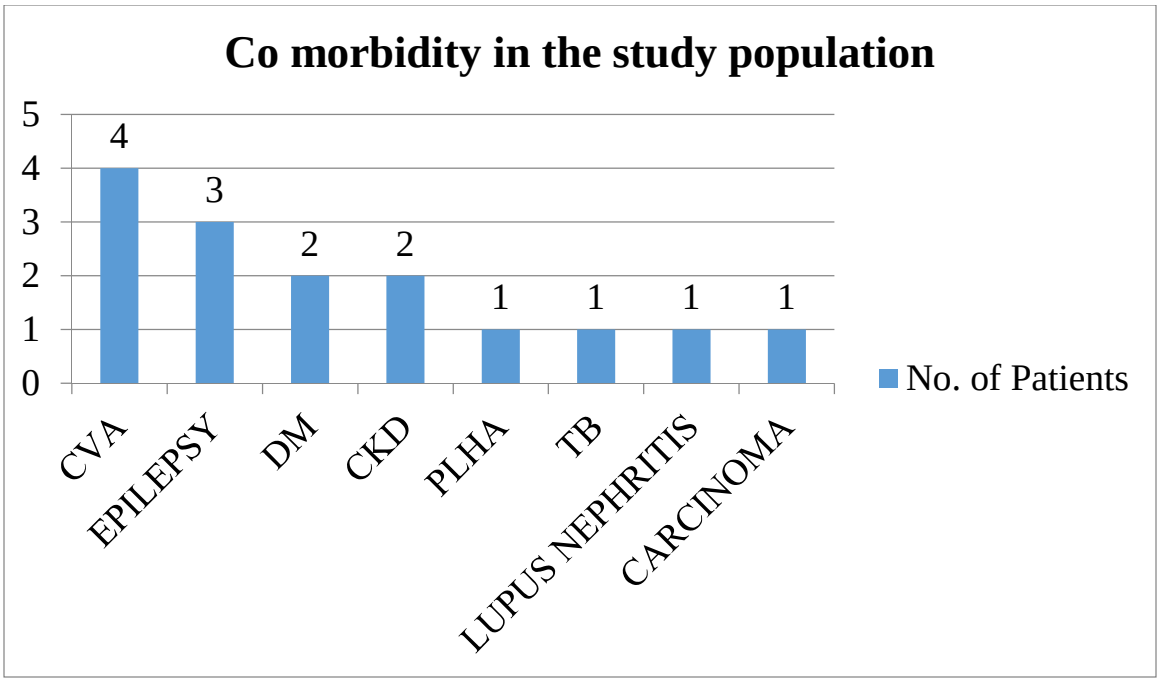

Figure 5: Co morbidity in the study population

The figure 5 states the co-morbidity of the study subjects. Among the total cases, 29.4% did not have any co-morbidity. CVA and epilepsy were the most common comorbidity being present in 7 of 17 patients (41.17%) in our study, followed by diabetes and CKD in two and SLE, lung carcinoma, HIV infection and Tuberculosis in one patient each.

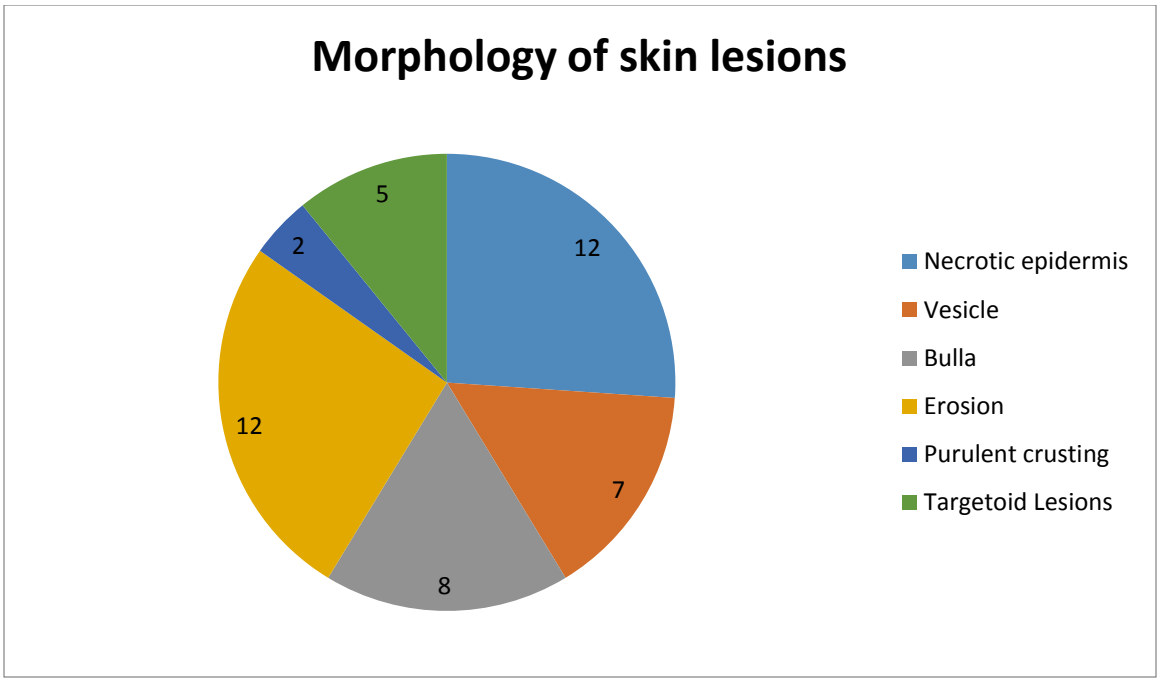

Figure 6: Morphology of skin lesions

Necrotic epidermis and erosion was the common finding, being present in 12 of 17 cases (70.58%). Vesicles and bulla occurred in 8 patients (47.05%). Purulent crusting over the erosion was seen in a PLHA patient with Toxic Epidermal Necrolysis.

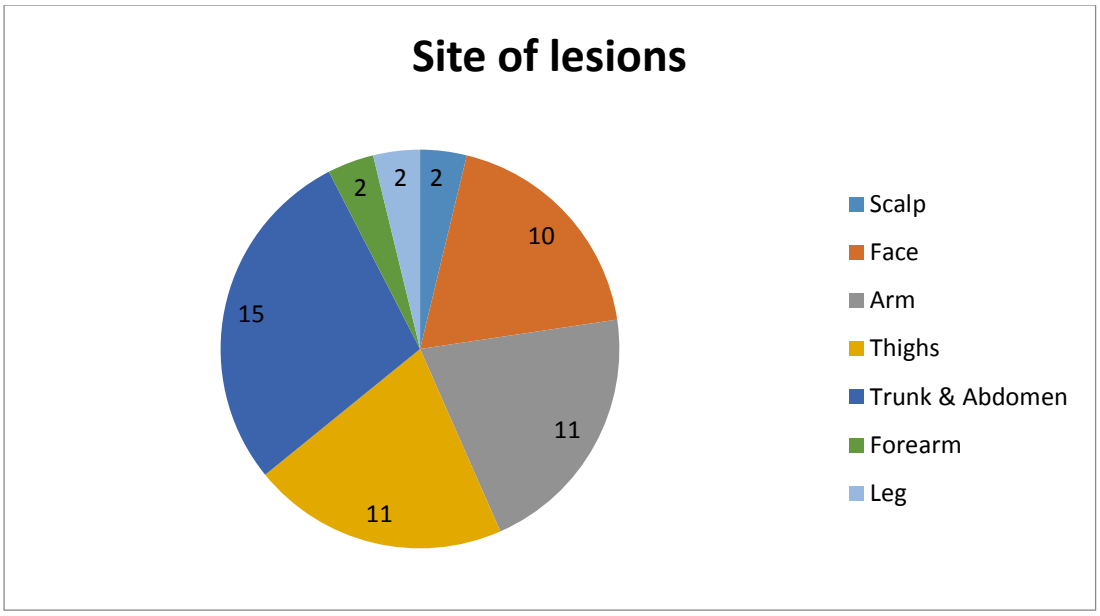

Figure 7: Site of lesions

Trunk and abdomen was involved in 15 cases (88.2%) followed by arms and thighs in 11 cases (64.7%) each. Scalp and face was involved in 2(11.8%) and 10 cases (58.8%) respectively. Forearm and leg was involved in 2 cases (11.8%) each. Scalp was spared in all patients of TEN, except one HIV positive patient who had 100% body surface area involvement. Distal extremities was the next common spared site in TEN patients, being uninvolved in 8 of 11 patients (72.72%). All 3 patients (100%) of SJS-TEN Overlap had involvement of trunk and proximal limbs.

BSA-Day 1 (%)	SJS		SJS-TEN overlap		TEN		Total	
	No	%	No	%	No	%	No	%
0	3	100	0	0.0	0	0	3	17.6
11-20	0	0	1	17.6	0	0	1	5.9
21-30	0	0	2	35.2	0	0	2	11.7
31-40	0	0	0	0.0	0	0.0	0	0
41-50	0	0	0	0	0	0	0	0
51-60	0	0	0	0	2	18.2	2	11.7
61-70	0	0	0	0	5	45.4	5	29.4
71-80	0	0	0	0	2	18.2	2	11.7
81-90	0	0	0	0	2	18.2	2	11.7
91-100	0	0	0	0	0	0	0	0
Total	3	100.0	3	100.0	11	100	17	100

Table-7: Body surface area on day-1 according to the diagnosis.

The day 1 body surface area of the study subjects was shown in the above table-7. The maximum number of cases 5 (29.4%) had 60-70 percentage BSA involvement.

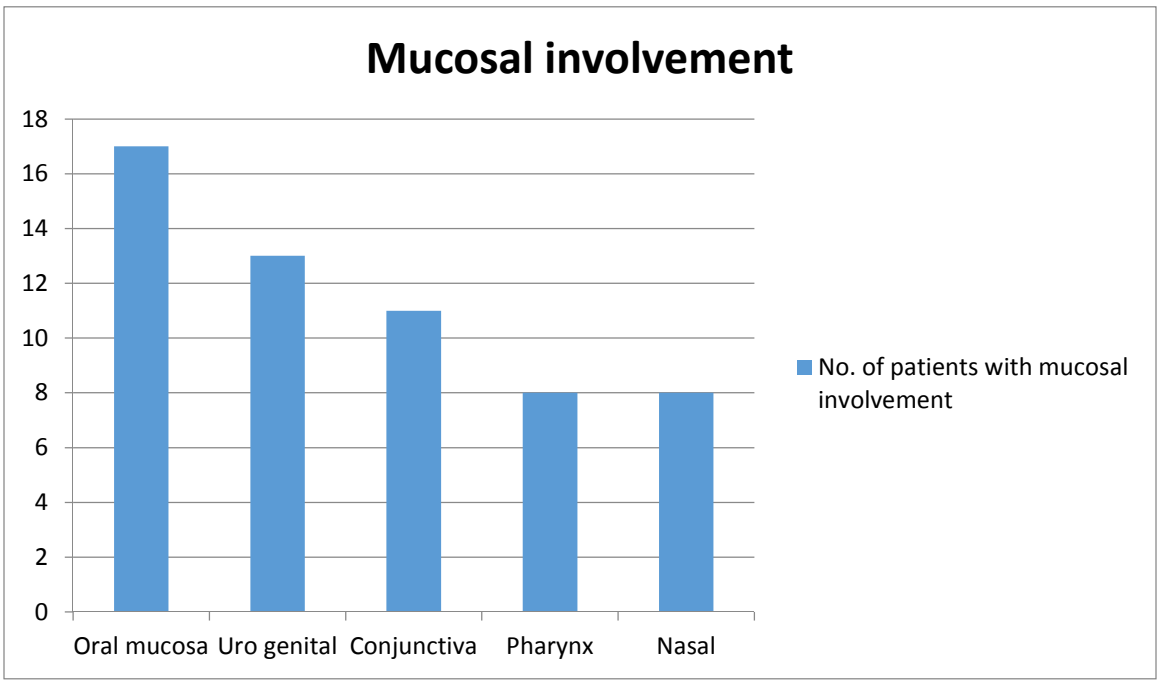

Figure 8: Mucosa involvement

The figure 8 states the mucosal involvement in the study cases. Cent percent of cases had oral mucosa involvement. The urogenital was next prevailing as in 76.5% of cases (13) and the conjunctiva in 11 cases (64.7%) followed by Pharynx and nasal mucosa in 8 cases each (47.1%).

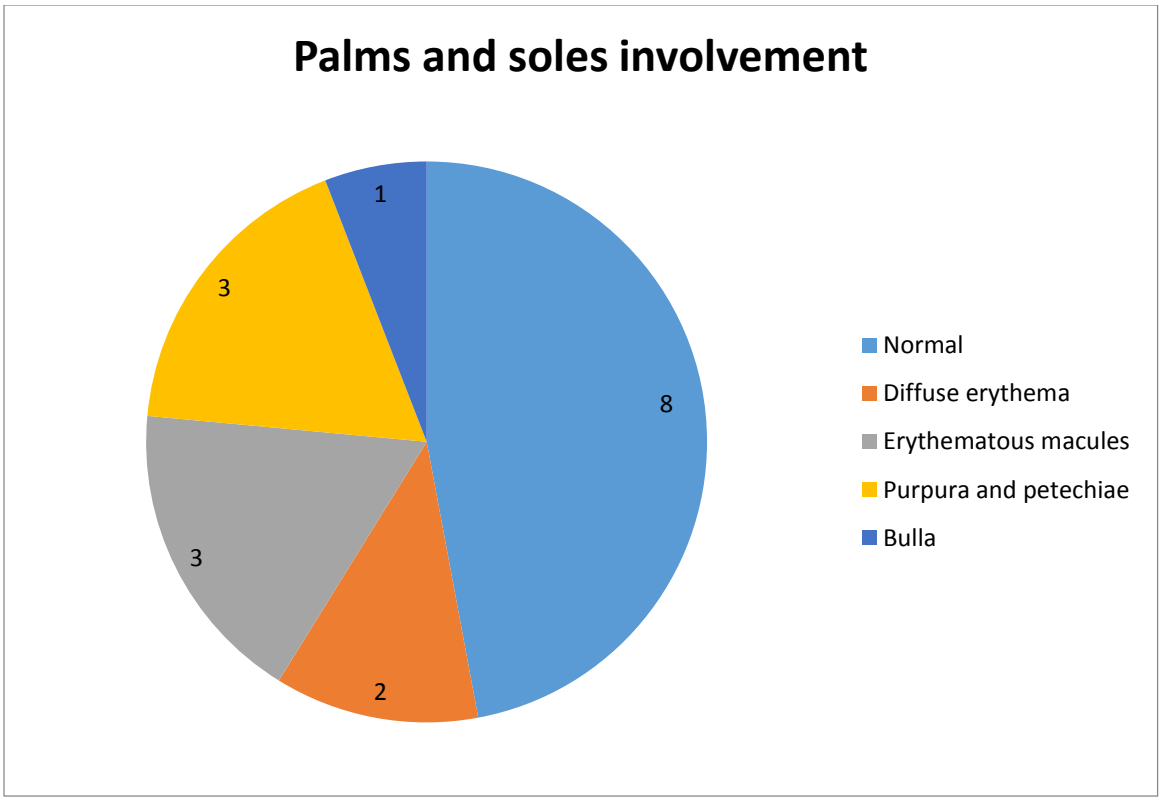

Figure 9: Morphology of lesions in palms and soles

The figure 9 states the morphology of lesions in palms and soles. Palms and soles were not involved in 8(47.1%) cases. Erythematous macules, petechiae and purpura were seen in 6 of 17 cases (35.2%), diffuse erythema was seen in 2 cases (11.8%) and bulla in 1(5.9%).

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Site	Diagnosis	N	Mean	SD	df	F	Sig
Skin	SJS	3	15.7	0.6	(2,14)	4.052	SJS Vs TEN ($p<0.05$)
	SJS-TEN overlap	3	11.0	4.6			
	TEN	11	10.6	2.5			SJS Vs SJS→TEN TENVsSJS→TEN $p>0.05$
	Total	17	11.6	3.2			
Mucosa	SJS	3	11.7	8.6	(2,14)	1.451	$p>0.05$
	SJS-TEN overlap	3	18.7	4.0			
	TEN	11	12.3	5.7			
	Total	17	13.3	6.2			

Table 8: Mean recovery time of skin and Mucosa

The mean recovery time of skin and mucosa was 11.6±3.2 days. In SJS, the mean recovery time was 15.7 ± 0.6 days and mean recovery time in TEN was 10.6±2.5 days. The difference was statistically significant ($p<0.05$). The mean recovery time of SJS-TEN overlap was 11.0±4.6 days. The difference between them was not statistically significant ($p>0.05$). In respect to the mucosa, the recovery time was prolonged for SJS patients than for TEN patient and the difference were not statistically significant ($p>0.05$).

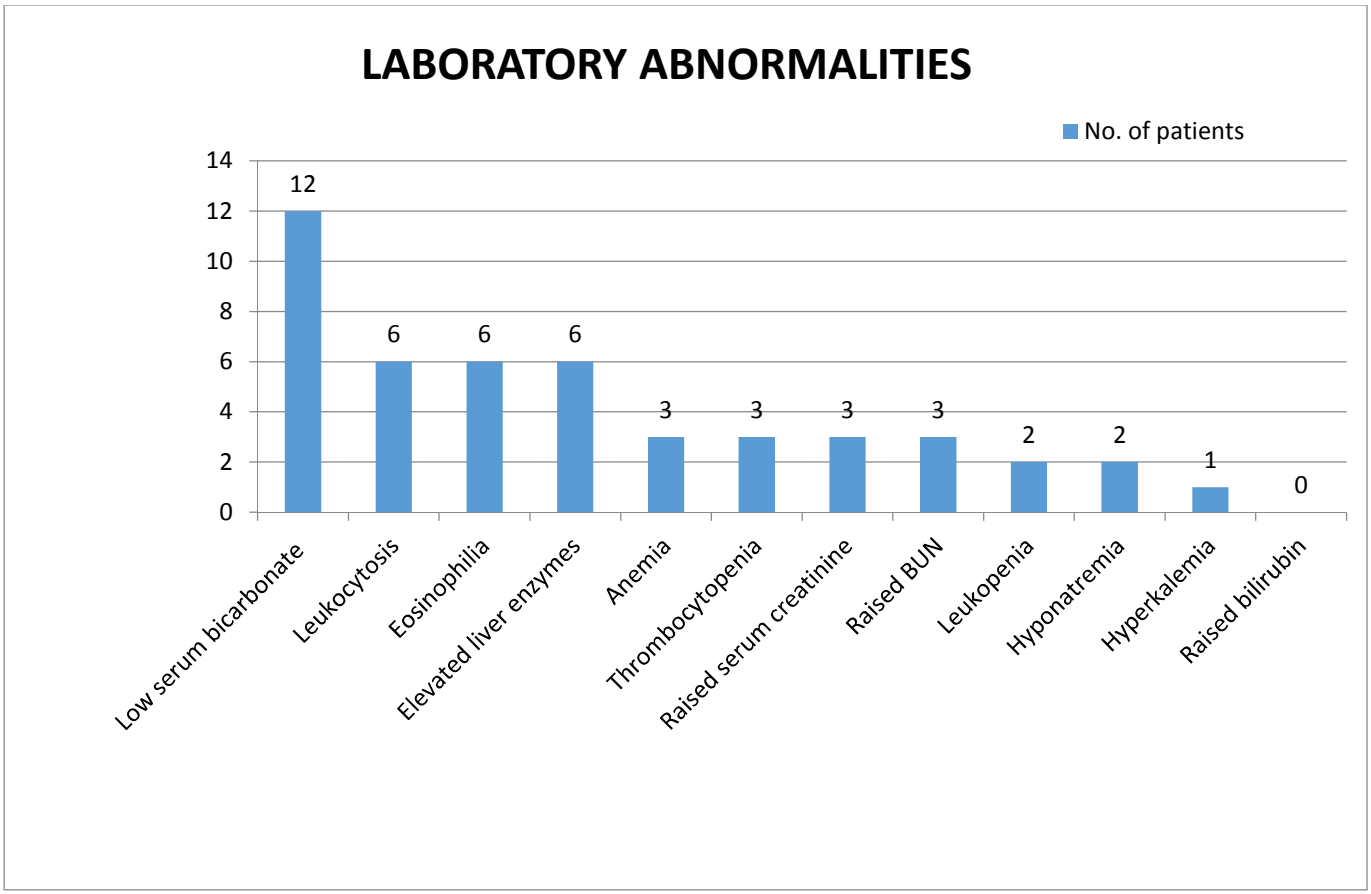


Figure 10: **laboratory abnormalities in the study subjects**

Change in total WBC count was the most common laboratory abnormality, being observed in 8(47.05%) of 17 cases, with leukocytosis in 6(35.29%) and leucopenia in 2(11.76%). Anaemia and thrombocytopenia was seen in 3 cases (17.64%). Elevated SGOT and SGPT was seen in 3(17.64%) of 11 TEN cases and 2(11.76%) SJS/TEN Overlap cases. Elevated SGPT and ALP was noticed in another SJS/TEN Overlap case. Among the 3 cases (17.64%) who suffered mortality, 2 cases (11.76%) of SJS-TEN overlap showed abnormal liver and renal parameters, whereas one case of TEN had liver parameter within normal range.

Renal parameters were elevated in 3 patients in our study and all the patients succumbed to death.

SCORTEN SCORING AND MORTALITY

SCORTEN was calculated for all patients on day 1, day 3 and day 5 of admission. The scores along with the outcome of individual patients have been recorded in the table 9.

S. NO	SCORTEN SCORE			MORTALITY
	DAY 1	DAY 3	DAY 5	
1	2	2	1	NO
2	2	3	2	NO
3	1	2	1	NO
4	3	3	3	NO
5	1	1	1	NO
6	1	2	1	NO
7	6	6	7	YES
8	2	2	2	NO
9	3	3	4	NO
10	3	3	2	NO
11	1	2	1	NO
12	2	1	2	NO
13	5	5	5	YES
14	4	4	5	YES
15	1	1	1	NO
16	2	2	2	NO
17	2	2	2	NO

TABLE 9: SCORTEN score (day 1, day 3 and day 5) and outcome of patients.

DAYS	SCORTEN VALUE (MEAN± S.D.)
DAY 1	2.471 (1.419)
DAY 3	2.647 (1.32)
DAY 5	2.529 (1.736)

Table 10: The mean scores on day1,3 and 5 are recorded in table 20

Kruskal Wallis test was performed to identify differences in the mean scores on days 1, 3, and 5. No significant difference was observed between the 3 groups.

DAYS	**SCORTEN VALUE (MEAN± S.D.)**	**Chi-square**	**dF**	**p value**
DAY 1	2.471 (1.419)	0.736	2	0.692
DAY 3	2.647 (1.32)			
DAY 5	2.529 (1.736)			

Table 11: Difference between SCORTEN values on day1, day3 and day 5

MORTALITY:

Of the 17 patients, 3 (17.64%) died, which included 2 patients of SJS-TEN overlap and 1 patient of TEN.

CATEGORY	NO OF PATIENTS	MORTALITY RATE(&)
SJS	3	0(0%)
SJS-TEN Overlap	3	2(66.66%)
TEN	11	1(9.09%)
TOTAL	17	3(17.64%)

TABLE 12: category wise distribution of mortality

CAUSE OF MORTALITY:

The cause of death in our patients is as shown in table 13.

DIAGNOSIS	CAUSATIVE DRUG	CAUSE OF DEATH
TEN	phenytoin	ARDS, SEPSIS,PRE RENAL AZOTEMIA
SJS-TEN Overlap	norfloxacin	AKI ON CKD/DKA
SJS-TEN Overlap	phenytoin	AKI ON CKD

TABLE 13: Cause of Mortality

CORRELATION BETWEEN SCORTEN AND MORTALITY:

SCORTEN	Expec. Morta %	SJS			SJS-TEN Overlap			TEN		
		cases	Mortality		cases	Mortality		cases	Mortality	
			Predic	OBS		Predic	OBS		Predic	OBS
0-1	3.2	2	0.064	0	0	0.0	0	0	0.0	0
2	12.1	0	0.0	0	0	0.0	0	8	0.968	0
3	35.3	1	0.353	0	1	0.353	0	2	0.706	0
4	58.3	0	0.0	0	1	0.583	0	0	0.0	0
≥ 5	90.0	0	0.0	0	1	0.900	2	1	0.9	1
Total		3	0.417	0	3	1.836	2	11	2.574	1

* Expec. Morta -> Expected Mortality, Predic.-> Predicted, OBS-> Observed

Table-14: SCORTEN validation:

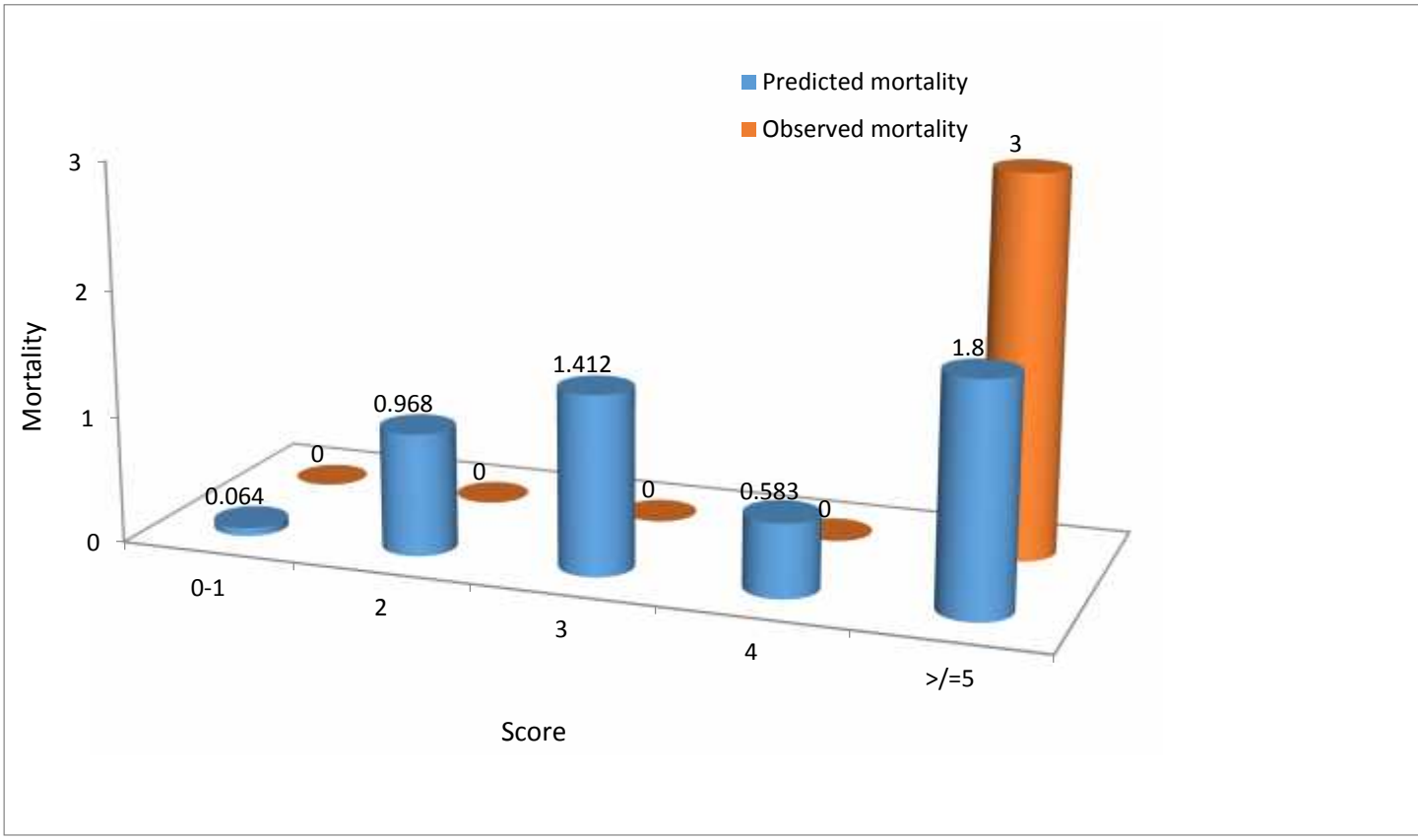


Figure 11: comparison between actual and predicted mortality

Figure 11 states that predicted mortality as well as observed mortality among the study subjects. The predicted mortalities were 0.417, 1.836 and 2.574 and the observed mortalities were 0, 2 and 1in SJS, SJS-TEN Overlap and TEN respectively. The predicted mortality was 4.827 and observed mortality was 3, with the scores of patients being 6, 5 and 4 (6 in TEN case and 5 &4 in SJS-TEN case).

The Standardised Mortality Ratio (SMR) of SJS-TEN Overlap was 1.1 and TEN was 0.389. The SMR of SJS-TEN Overlap was statistically significant ($p<0.05$) and the SMR of TEN was not statistically significant ($p>0.05$).

Correlation between SCORTEN and mortality	Correlation coefficient	p value
DAY 1	0.653	0.008
DAY 3	0.571	0.026
DAY 5	0.893	<0.001

Table 15: COMPARISON BETWEEN ACTUAL AND PREDICTED MORTALITY

From the above table, it is clear that SCORTEN correlates significantly with mortality on all the 3 days in our study.

Sl No	Factors	Alive n=14	Death n=3	Total n=17	Exact Sig
1	Age above 40 years	5	3	8	p>0.05
2	Cancer	0	1	1	p>0.05
3	Heart Rate above 120	0	2	2	p<0.05
4	Epidermal detachment above-10%	11	3	14	p>0.05
5	BUN above 28%	0	3	3	p<0.01
5	RBS > 252mg	0	2	2	p<0.05
7	Se HCO 3 <20mmol/L	9	3	12	p>0.05

Table-16: Univariate analysis of Individual Factors of SCORTEN on mortality

The table -16 associates the SCORTEN factors, parameter wise with the alive and dead subjects. The factors namely age above 40 years, cancer, epidermal detachment above 10% and Se HCO3 <20 did not associate significantly with the mortality (p>0.05). The heart rate above 120/min and RBS>252mg% were associated significantly with the death of the subjects (p<0.05). The BUN above 28% was highly associated with death (p<0.01) in our study.

DISCUSSION

Stevens- Johnson syndrome and Toxic epidermal necrolysis are life threatening severe cutaneous adverse drug reaction (SCAR) and is one of the most important dermatological diseases which cause mortality. Knowledge of SJS and TEN is needed not only for Dermatologist, but also for physician and Opthalmologists for its effective management. Controversies exist not only about the etiology, but also the diagnosis, classification and appropriate treatment of this disorder. Due to the rarity of its occurrence, most of our current knowledge is based on small case series and case reports. There have been only a few large scale studies evaluating the etiological agents and clinical features of SJS & TEN in Indian context. As regards the management, various therapeutic agents in use are corticosteroids, intravenous immunoglobulins, cyclosporine A, and plasmapharesis. Conflicting evidences still continue whether conservative management including meticulous inpatient monitoring or the use of immunosuppressants like steroids or other agents are essential in the management. Also, as this is one drug reaction which carries a significant mortality rate, it is important to predict the mortality early and treat the patient accordingly. However, a clear consensus of management in relation to the severity is still lacking.

Measuring the severity of illness and predicting the mortality needs a specific scoring system. And such an illness severity score formed subsequently is

SCORTEN. It was developed and validated in Europe by Bastuji-Garin et al as a predictor of mortality. It is currently being used worldwide to predict the probability of hospital mortality and to determine the efficacy of therapeutic interventions. There are studies going on in various parts of the world to evaluate its usefulness in their particular areas, as genetic factor is an important count in the occurrence and prognosis of SJS and TEN patients.[7,8,129-134] There have been only a very few studies evaluating the applicability of SCORTEN in Indian population and to the best of our knowledge there are no published studies confirming its validity in South Indian patients.

Study by Vaishampayan et al and Sekula et al have raised the need for re-evaluation of the existing SCORTEN parameters and have also suggested few modifications to the original scale.[10,15] Imahara et al have found that the predicitive performance of SCORTEN is influenced by the treatment protocol used and Spornraft Ragaller et al have observed that SCORTEN did not perform well in severly affected patients.[135,136]

The present study aimed at studying the clinicoetiological profile and outcome of SJS & TEN patients and to confirm the accuracy of SCORTEN in predicting the mortality in Indian patients by serial analysis on day1, day3 and day5 of admission.

A total of 69 cases of drug reaction were reported during the study period including 19 cases which fell under SJS & TEN spectrum. This relatively high incidence (29.53%) of SJS-TEN spectrum in our study was similar to a retrospective study by Sushma et al on 404 hospitalised patients over a 9 year period, who also showed a higher incidence (19.5%) of SJS & TEN spectrum in South India when compared to other countries.[137]

A total of 17 cases of Stevens Johnson syndrome and Toxic Epidermal Necrolysis and its Overlap were included in the study. Among this 3 patients fell in SJS spectrum, 3 in SJS-TEN overlap and 11 patients in TEN spectrum. The age of our patients ranged from 11 to 67 years, with mean age among males was 39.2±18.4 years and the same of the females was 35.5±24.7 years. This was in accordance with a study by Roujeau et al, where the majority involved was in the age group of 40-50 years. This was in contrast to few other Indian studies by Kaur et al and Sharma et al, where the mean age was 23 and 22.3 years respectively.[16,18,26]

The youngest and oldest patients in our study were 11 and 67 years respectively, although this disease has been reported to occur in extremes of age ranging from 1-93 years. In recent Indian studies by Sharma et al and Devi et al the age range of patients were from 4 to 74 years.[17,18]

Most of the patients, 7(41%) in our study were in the age group of 30- 50 years. In 11 patients (64%) the age of onset was after 30 years and in 4 patients (23%) the onset was after 60 years, supporting the view that the incidence increases with age. Age is one among the prognostication factor in SCORTEN. The largest EuroSCAR study shows that the death rate is lower in children than in elderly. In the EuroSCAR study the death rate correlated strongly with the patient's age and to the severity of the disease, whereas in our study the incidence increased with age, but not the mortality.[118] This is in contrast to a 27 year retrospective study by Oen et al, which shows advanced age is associated with mortality.[138]

Our study showed a male preponderance, with a male: female ratio of 3.25:1. Male preponderance has also been seen in few of the previous studies by Ting et al and Shah et al.[37,38] This is in contrast with some of the recent studies, where equal incidence in male and female was reported. A higher incidence in female was reported by Roujeau et al in their retrospective study of 253 patients with male female ratio being 0.6:1.[26] This male preponderance in our study may be due to the disparities in the availability of health care access and increased opportunity to attend tertiary care centre by males.

Our patients presented within 1-6 days of onset of symptoms (median 3 days). Majority of the patients, 8 cases (47.95%) presented within first 3 days of onset. This was comparable with the original study by Bastuji-Garin et al, for the

development of SCORTEN where the mean day of hospitalization after the onset of symptoms was 2 days.[25] The period of delay in hospitalization showed no significant impact in the final outcome of patients in terms of mortality in our study ($p>0.05$). This was consistent with the finding of Guegan et al, who also did not find any significant effect of admission delay on the prognosis of the patient.[7]

In 8 patients (47%) mucosal lesions preceded the skin lesions, whereas in 7 cases (41.7%) skin lesions were the first and in 2 cases (12.76%) simultaneous onset was noted. In a study by Roujeau et al, mucosal lesions preceded the skin lesions by upto 3 days in one-third of the cases.[26]

On the skin, trunk was the first site of involvement in 12 of 17 patients (70.58%), whereas in case of mucous membrane, the oral mucosa was the first to be involved in 16 of 17 patients (94.11%) and oral mucosa was involved in 100% of patients.

Most of our patients,12 (70.58%) presented with history of prodromal symptoms in the form of fever, malaise, conjunctivitis and sore throat, 1-5 days before the onset of mucocutaneous lesions. Fever and malaise was the most common prodrome in 7 of 17 cases (41.76%), followed by conjunctivitis, URI and cough. Pyrexia has also been reported in most of the patients by Kaur et al and Ting et al in their respective studies.[16,37]

Cutaneous prodrome occurred in the form of itching, burning sensation and skin pain. Cutaneous prodrome was positive in 9 of 17 cases (53%). All the patients who had skin pain as prodrome ultimately developed Toxic Epidermal Necrolysis. This inference has not been highlighted in any other studies published so far. The skin pain before the onset of TEN may be due to subclinical keratinocyte necrosis. In patients with 2nd episode of this severe type of reaction to analgesic, burning sensation and skin pain occurred within 12 hours of single dose of tablet aspirin caffeine combination and after 30 minutes of single dose for T. Ibuprofen.

A positive history of drug intake was obtained in 100% of our study population in the preceding 3 weeks. This was in accordance with most of the recent studies. Regarding the other possible etiological factors, URI was present in 3 cases (17.64%). It was difficult to decide whether that was a part of symptomatology of SJS and TEN or the cutaneous reaction is in itself due to the preceding infection. Ting et al reported similar finding in their study, in 15% of the patients. However, in contrast to their study, none of our patients had a history of herpes simplex, dental abscess, vaccination or irradiation or pregnancy in our study.[37]

Most of our patients had received more than 1 drug prior to the onset of the disease, similar to the findings by Guillaume et al.[139] A single culprit drug could be

determined in 15 out of 17 cases ie 88% of patients in our study. In patient who was on Cat I ATT, the single etiologic agent could not be identified. And in one patient, only a history of analgesic intake was elicited, but the exact drug was not found out.

Anticonvulsant was the commonest drug implicated as a cause of SJS/TEN in 47% of cases, followed by analgesic in 35%, antibiotics in 11% and ATT in 5.88% of patients. This was in accordance with other Indian studies by Sharma et al and Devi et al who also reported anticonvulsant as the commonest causative drug in 35% and 53% of the patients respectively.[17,18]

Phenytoin was the commonest anticonvulsant involved in 29.4% followed by carbamazepine in 18% of cases in our study. This is similar to a study by Sharma et al where also phenytoin was the commonest anticonvulsant implicated.[18] But Kim et al, Devi et al and the largest EuroSCAR study proved that carbamazepine was the most common anticonvulsant in SJS/TEN spectrum.[17,108,118] In a study by Bansal et al, phenytoin and carbamazepine were equally responsible.[107] All patients who developed reaction to anticonvulsants were safely put on T. Levetiracetam with no reaction to it. This may be because levetiracetam is structurally unrelated to the existing anticonvulsants, most of which have the aromatic ring. No case report of SJS/TEN is noted with levetiracetam in the studies

published so far. So, levetiracetam can be considered, the safe alternative anticonvulsant.

Amongst the analgesics, 2 of the 6 cases (33.33%) were due to T. Aceclofenac and both were SJS. Other 4 cases were due to T. Ibuprofen, T. Aspirin + Caffeine combination, Paracetamol suppository and 1 unidentified analgesic. This is similar to a recent study by Lihite et al, who also reported 24.45% of patients developed reactions to analgesics like aspirin, ibuprofen, paracetamol, etoricoxib.[140] Roujeau et al reported that among NSAIDS oxicam and pyrazolone derivatives are the leading cause of TEN.[26]

Antibiotics were the causative agent in 11% of cases (2 of 17 cases). This is similar to the recent study by Bansal et al and incontrast to many older studies where antibiotics especially sulfonamides were implicated as the commonest culprits.[107] Decreased use of sulfonamides due to the advent of newer antibiotics may be the reason for reduced incidence of SJS and TEN to these drugs. Among antibiotics TEN was noted in one patient on Inj ampicillin and SJS-TEN Overlap symptoms was seen in another patient on T. Norfloxacin. One of our patients was on Cat I ATT before the onset of reaction. ATT drugs have been reported as the most common offending agent in a study of 30 patients by Kaur et al.[16] In anti-tubercular drugs, there are individual case reports of SJS and TEN occurring to thiacetazone, streptomycin, PAS, pyrazinamide and isoniazid . Among the

Category I ATT, isoniazid and pyrazinamide have been commonly reported to cause SJS and TEN.[141] However Chaudry et al have published a case report of TEN to Ethambutol in his study.[142]

The time interval between drug administration and onset of disease ranged from 1 day to 40 days. Phenytoin had the longest duration, for the reaction to start with mean being 33 days whereas to carbamazepine it was 11 days. The presentation in both cases were TEN and SJS. 3 patients developed exfoliative dermatitis to carbamazepine during the study period. The mean duration of drug intake in them was 42 days, in contrast to SJS and TEN, where it was 11 days. This indicates that each morphology of drug reaction has a specific sensitization period. Also the sensitization period varied among different group of drugs.

The duration between drug intake and onset of reaction was shorter with antibiotic and analgesic with a mean of 7 days for antibiotics and 5 days for analgesics.

During the second episode, we observed that the time interval between drug intake and reaction was longer for anticonvulsants (40 days) in contrast to analgesics where it was shorter (<12 hours). Also we found that the reaction was milder with anticonvulsants and severe with analgesics. This finding throws some lights regarding the utilisation of desensitization phenomena which could be tried

in future with controlled administration of anticonvulsants in patients with reaction. But the same cannot be applied for analgesics. This observation has not been mentioned in any other studies published so far.

A case of Carcinoma lung with brain metastases treated with radiotherapy developed TEN to phenytoin. This was in accordance with the findings reported by Aguiar et al and Gomex-Criado et al, who found that the patients with brain tumors treated with radiation appear to be more susceptible to SJS/TEN when given phenytoin.[29,30]

Most of our patients (12 cases, 70.58%) stopped the drug early within 3 days of onset of reaction with no delay in recognition of reaction in 6 cases (35.29%). This was probably due to increased awareness about the possibility of drug reaction in our patient and early available access to medical facility for timely intervention. The delay in other cases were due to delay in hospitalization except in one case of TEN to rectal paracetamol suppository in a child, a delay of 4 days was due to decreased degree of suspicion towards the drug.

On examination, fever was present in 7 of 17 cases (41.2%), Tachycardia in 2 patients (11.76%), Tachypnoea in 6 (35.29%), Crepts and Pneumonitis in 2 patients (11.76%). In chest X ray, infiltrate was seen in 3 patients (17.64%) and 2 of these 3 cases succumbed to death. d et al have suggested respiratory

involvement as a poor prognostic factor in SJS/TEN that is not reflected in SCORTEN, and have recommended a further validation of SCORTEN in these patients.[14]

The classical morphology and distribution of mucocutaneous lesion described for SJS and TEN was seen in most of our patients. The predominant sites of involvement were the trunk and proximal extremities in 100% of cases. This was consistent with the consensus case definition of EM, SJS and TEN by Bastuji Garin et al, who also differentiated SJS/TEN from EM by predominant truncal and proximal limb involvement, in contrast to the predominant acral involvement in classical EM.[25]

81.8% of our patients presented with necrotic epidermis and 47.1% had bulla and erosions. Thick adherent purulent crusted plaques with fissures and scalp involvement was noticed in a HIV positive TEN patient in our study. This is in contrast with Roujeau et al, who have reported that even in patients with severe skin involvement; the hairy portion of the scalp is typically spared in TEN.[143]

The area of epidermal detachment was calculated in all patients according to the Wallace rule of nine on day1, day3 and day 5 of admission. The final classification of the patients as SJS, SJS-TEN Overlap or TEN was done according to the percentage of body surface area detachment on day 1 in our study, in

contrast to Bansal et al who classified the patients on the basis of BSA involvement on the worst stage of the disease.[107] Based on this we had 11cases of TEN, 3 cases of SJS-TEN Overlap and 3 cases of SJS. A rapid increase in the percentage of detached epidermis was observed over time. While there were 11 patients (64.7%) with more than 30% detached epidermis on day 1, it was 13(76.5%) in day 5, as reported by many other authors. This also supports the fact that SJS can evolve into TEN and the two diseases form a clinical spectrum, rather than being distinct disorders. But in our study no change in spectrum over days is noted. In 4 patients (23.52%) almost 100% of the epidermis was detached on day 5. Except one patient with 100% BSA involvement in day 5, who suffered mortality all the others revived. The area of BSA involvement did not affect prognosis much in our patients. This may be due to the barrier nursing, meticulous supportive and wound care given.

Nikolsky and Skin tenderness was present in 14 of 17 patients (82.35%) on the day of admission. All patients in our study had mucosal involvement (100%). In majority of the patients, 15(88.23%) had more than one mucosal site involvement.

Many of our patients had deranged hematological and biochemical parameters as reported by Goens et al.[106] Anaemia was present in 3 patients (17.64%), leucopenia in 2 (11.76%) and leukocytosis in 6 patients (35.29%).

Similarly, leukocytosis and leucopenia has also been reported in 24% and 6% of the patients respectively in a study of 34 cases by Ting et al.[37] Thrombocytopenia was seen in 3 cases and all the cases suffered mortality in our study. So this could be considered as one of the prognostic factors. This observation has not been encountered in any of the studies published so far.

Six patients had elevated liver enzymes in our study, while 4 survived, 2 patients who had associated BUN elevation succumbed to death.

Renal involvement in the form of raised serum creatinine was present in 3 cases (17.64%) in our study. Raised serum creatinine was also found in 29% of total patients studied by Ting et al. The elevated BUN: creatinine ratio is suggestive of pre renal azotemia. Renal function impairment was shown to be associated with negative survival in the study by Kim et al and Bansal et al.[107,108] The main cause of renal failure in SJS/TEN is defective barrier function of the stratum corneum leading to increased fluid loss and pre-renal acute kidney injury. Hence timely correction of hypovolemia by appropriate fluid management must be a priority in all cases of SJS and TEN.

In our study, 2(11.76%) patients progressed to acute renal failure and both of them died. In a study of 96 cases by Hung et al, 20.8% of the patients progressed to acute renal failure. The authors have also identified sepsis, NSAIDs, antibiotics,

chronic kidney disease and hypoalbuminemia as independent risk factors for development of ARF in patients of SJS/TEN.

Electrolyte derangement were seen in the form of hyponatremia , hyperkalemia in 2(11.76%) and 1(5.88%) of our patients respectively. Hung et al have also reported hyponatremia and late hypokalemia in 15.6% and 7.3% of the patients respectively.[144] The authors also found a positive association of electrolyte derangements with certain drugs like NSAIDs, anticonvulsants and allopurinol. Hypokalamia persisted from 2 weeks to 5 years in their patients and potassium supplement was needed. Larger studies are required to corroborate these findings which can have a significant effect on the final outcome of the patients.

70.58 percent of our patients (12) had a low serum bicarbonate (<20mEq/L). The primary cause of low bicarbonate is hyperventilation and subsequent respiratory alkalosis. Kidneys compensate for the alkalosis by losing bicarbonate causing a metabolic acidosis. Serum bicarbonate <20mEq/L is one of the 7 parameters included in SCORTEN, which independently affects mortality, as also seen in our study ($p<0.05$).[145]

Skin, blood and urine culture sensitivities were done for all patients. Septicemia was confirmed in 1 patient with positive growth on blood culture. Staphylococcus aureus was the organism grown. Kaur et al reported septicemia in

20% of patients they studied.[16] The organisms grown were staphylococcus aureus, klebsiella pneumonia and Pseudomonas aeruginosa.

In our study, 2 patients (12%) had positive skin culture and the organisms grown were Staphylococcus and klebsiella. Staphylococcus was isolated by Kaur et al and Bansal et al.[16.107]

Co existing morbidities were present in 10(58.82%) cases in our study. 3 patients (17.6%) suffered mortality in our study. All three patients who died had a score of 6,5 and 4 on day 1. All the patients were above the age of 40 years. All had elevated BUN and thrombocytopenia, 2 patients had infiltrate on chest Xray and elevated liver enzymes along with BUN rise. 2(11.76%) patients who suffered mortality had Chronic Kidney disease with additional co-morbidity of Diabetes in one patient and CA lung with secondaries brain in another patient. And the last patient also had ARDS and pre-renal azotemia. Thus, elevation of renal parameters has been an important predictor of mortality in our study and it should be given more score in future studies.

Of the survivors 7 of 14 (50%) had co-morbidities, in the form of epilepsy in 2 and diabetes, AIDS, Tuberculosis, CVA and SLE in one each. Bastuji Garin et al state that AIDS is not usually associated with poorer hospital prognosis among TEN patients, which is proved in our study.[5] Pre-existing circulatory co-morbidity

has shown a relatively high risk of decease in a study by Oen et al.[138] However, in our study, we did not encounter circulatory or cardiovascular co-morbidity in any of our patients. Studies by Devi et al and Vaishampayan et al also reported a high incidence of co-existent morbidities in Indian patients in their respective studies.[10,17]

SCORTEN was calculated for all 17 patients on day1, day3 and day 5 of admission in our study. The mean SCORTEN value on day1, day 3 and day 5 were 2.471, 2.647 and 2.529 respectively. Kruskal Wallis test was employed to identify the difference in predictive value of SCORTEN on these three days. In our study, no significant difference was found in the predictive value of SCORTEN on the three days. This is similar to the original study proposed by the authors where SCORTEN is performed within 24 hours of hospitalization and a Taiwanese study by Ho et al.[132] In a study on 144 patients bu Guegan et al, SCORTEN was found to perform best on day 3 rather than on day 1.[7] This is in contrast to our study as others like Bansal et al and Vaishampayan et al, who found that the SCORTEN performance was best on day 5.[10,107] This variation in the performace of SCORTEN may be due to the mean delay in hospitalization which varies in each studies.

Further, we also analysed the difference in SCORTEN values between alive and dead patients and assessed whether the actual mortality in patients with a

particular score value in SCORTEN was comparable with the mortality predicted for that particular score.

On comparing actual and predicted mortalities, it was observed that the overall actual mortality was comparable to the predicted mortality by SCORTEN on all 3 days. The discriminative power of SCORTEN was acceptable for all 3 days calculated, as similar to Bansal et al.[107]

On calculating the standardized mortality ratio (SMR), SCORTEN scoring was statistically significant for patients of SJS-TEN Overlap (SMR>1). In TEN patients, SMR was 0.389, with the observed and predicted mortality being 1 and 2.574 respectively. Thus, SCORTEN gives an overestimation of mortality in patients falling in severe end of spectrum. This is similar to an observation by Spornraft Ragaller et al, who also found that SCORTEN did not perform well in severely affected patients.[135]

On univariate analysis of individual factors in SCORTEN, BUN >28mg% was more significantly associated with mortality in our study ($p<0.01$) followed by heart rate >120/mt and RBS>252mg% which were significantly associated with the mortality ($p<0.05$). This was similar to a study by Kim et al, where on univariate analysis, kidney function abnormality, pneumonia and anemia showed significant negative correlation with survival.[108]

Another factor associated with a significant fatal outcome in our study was penumonitis as similar to the study by Hague et al. But this is not reflected in SCORTEN.[14]

Percentage of body surface area detachment did not influence the mortality in our study. 4 patients had 100% body surface area detachment at some point of hospitalisation. Proper supportive care and barrier nursing helped them to recover completely. This is in discordance with the study by Vaishampayan et al, where BSA detachment >30% was associated with significant increase in mortality compared to BSA >10%.[10]

Thus we conclude that certain additional parameters should be considered while estimating mortality in Indian set up especially septicemia, combined elevation of liver and renal parameters and respiratory involvement. Also certain modifications need to be made in the existing SCORTEN, like

1. Giving a score of 2 to the elevation of BUN
2. Giving a score of 3 to patients having elevation of liver enzymes along with BUN rise
3. Considering thrombocytopenia as one parameter

The day of admission of the patient varied from 1 to 6 days after the onset of the disease in our study. This also can interfere with the validity of SCORTEN.

In our study, 3 patients (17.64%) succumbed to death while 14(82.35%) survived. Intravenous steroid therapy was preferred as the main treatment regimen in this study, along with conservative management including fluid and electrolyte replacement, nutritional support, temperature regulation, daily dressings and prophylactic antibiotics. Intravenous Immunoglobulin was given in one child case. N acetyl cysteine capsule was given in 3 patients, who showed a rapid re-epithelisation. There were no complications from steroid treatment in our study. Thus, we found that early steroid therapy with supportive management is beneficial in the management of SJS and TEN. This is in accordance with a study by Kim et al.[108] The recent IADVL therapeutic guidelines proposed in the year 2016 by Gupta et al also recommends, early (preferably within 72 hours) initiation of moderate to high doses of oral or parenteral corticosteroids (prednisolone 1-2mg/kg/day or equivalent), tapered within 7-10 days with supportive care.[113]

Prins et al and Trent et al concluded that IvIg is safe and effective in SJS and TEN.[8,119] Whereas Schenck et al reported no benefits from IvIg.[118] In our study, we used IvIg for one child case at a dose of 1g/kg and the the patient showed rapid improvement after IvIg. A recent study by Bansal et al recommends

only conservative management without immunosuppressants as a valid therapeutic option.[107]

The overall mortality in our study was 3(17.64%) which was higher for SJS-TEN Overlap (66.66%) as compared to TEN(9.09%) . None of the patients with SJS died in our study. Mortality rate ranging from 10-70% has been reported in various studies. An overall mortality rate of 16.7% is observed by Bansal et al as similar to our study.[107] All of our patients who died, 3/3(100%) had an underlying systemic illness in the form of Chronic renal disease, Diabetes and Lung cancer.

The time taken for complete recovery time of skin ranged from 11.6±3.2days and mucosa 13.3±6,2days. Bansal et al have reported a mean duration of 21.7 days for complete recovery in their study on 30 cases.[107]

About the long term sequelae, pigmentary disturbances were seen in 13 of 14(92.85%) survivors during follow up. Hyperpigmentation was the most common pigmentary change in our study. Pigmentary alterations have been reported in 66.7% cases studied by Revuz et al.[36]

In eyes, dry eyes and grittiness was noticed in 5 of 14(35.71%) surviving cases. This is similar to studies by Revuz et al and Yip et al, where ophthalmic complications was reported in 40-60% of the patients, with the changes being dry eyes and grittiness as our study.[36,146]

One patient developed, palmoplantar psoriasis after 3 months of TEN in our study and this observation by us has not been reported in any case reports or literature so far.

One patient developed phimosis upon healing of genital erosion which was reduced surgically. Symblepharon was noted in another patient during acute episode which was released surgically. The same observation was also made by Bansal et al in his study.[107]

Long term sequelae occurred in more than 50% of the survivors in the study of Haber et al and Oplatek et al.[147,148]

The limitation of this study includes the fact that the etiologic agents were determined by history and not by Immunologic analysis. Treatment patterns differed among patients. Owing to the small sample size, statistically significant conclusions could not be derived from our study. Also, our study did not include genetic susceptibility testing to SJS and TEN. Routine genetic testing if done can alter the etiologic profile of SJS and TEN and thus decrease its incidence. No strict steroid regimen and dose tapering was followed in our study and the treatment was individualized to each patient based on their response.

Thus we conclude that although SJS and TEN are severe life-threatening drug reactions associated with a poor prognosis, appropriate and timely

management of the patients in a tertiary care set up can significantly reduce the mortality and shorten the course of illness.

We also conclude that the performance of SCORTEN in our study showed no difference between day 1, 3 and 5. Hence, doing it on one day will provide valuable information regarding the prognosis.

We also suggest certain modifications could be done in the existing SCORTEN, based on the observation made in our study.

A modified SCORTEN is proposed by us for South Indian patients as follows:

1. Blood urea nitrogen above 28mg/dl – 2 (or)
   combined elevation of liver enzymes with BUN >28mg/dl - 3
2. Tachycardia (heart rate more than 120 beats per minute) - 1
3. Random blood sugar >252mgs - 1
4. Presence of malignancy -1
5. Presence of pneumonitis / Chest X-ray infiltrates -1
6. Thrombocytopenia – 1
7. Age > 40 years – 1
8. BSA involvement on Day 1 >10% - 1
9. Serum Bicarbonate level <20mmol/L - 1

On univariate analysis, BUN >28mg/dl was highly significantly associated with the mortality followed by tachycardia and blood sugar in our study. All 3 patients who died had co-morbidity and all 3 went into pre renal azotemia during the course of illness. Six patients had elevated liver enzymes in our study, while 4 survived, 2 patients who also had associated BUN rise succumbed. Thus, combined elevation of liver enzymes and BUN is suggested to give a score of 3. Pneumonitis was observed in 2 of 3 patients who suffered mortality and thrombocytopenia in all 3. Although increased incidence of SJS & TEN with age was noted in our study, there was no correlation of age with the mortality. Similarly, patients with entire body surface area involvement improved well and BSA did not affect mortality in our study. This may be due to the role of treatment, as similar to the observation by Imahara et al. Thus the predictive performance of SCORTEN is influenced by the treatment protocol used. And many patients had decreased bicarbonate in our study and the fall in bicarbonate was also not significantly associated with the mortality. So the validity of these parameters in predicting mortality need to be assessed in future large scale studies. Thus according to the modified SCORTEN proposed by us, the scores of the patient who died on day 1 were 8, 9 and 9.

Also use of SCORTEN in modifying the therapeutic regimen can be tried in future.

However, in view of paucity of prospective/controlled studies on SJS and TEN and lack of studies confirming the validity of SCORTEN in Indian patients, studies analysing larger sample size are needed to validate our study.

CONCLUSIONS

SJS and TEN are severe life-threatening drug reactions associated with poor prognosis. The clinical and etiological profile of the patients in our study is similar to the standard literatures. Appropriate and timely management of patients in a tertiary care set-up can significantly reduce the mortality and shorten the course of illness. SCORTEN is a prognostication tool, based on a minimal set of well-defined variables proposed by Bastuji-Garin et al in 2000. But its predictive ability varies with the population. We assessed the performance of SCORTEN in South Indians and have proposed certain modifications based on our observations. Single day analysis is as good as the serial analysis and will yield a reliable estimate of mortality which is cost-effective in resource poor settings. SCORTEN gave a significant estimation of mortality in SJS-TEN Overlap patients, whereas it gave an overestimation of mortality in TEN patients.

Modified SCORTEN for Indian patients proposed by us, is as follows:

1. Isolated Blood urea nitrogen above 28mg/dl – 2 (or)

   Combined BUN rise associated with liver enzymes rise - 3
2. Tachycardia (heart rate more than 120 beats per minute) - 1
3. Random blood sugar >252mgs - 1
4. Presence of malignancy -1

5. Presence of pneumonitis/ chest X ray infiltrates -1
6. Thrombocytopenia – 1
7. Age > 40 years – 1
8. BSA involvement on Day 1 >10% - 1
9. Serum Bicarbonate level <20mmol/l - 1

We recommended a conservative approach of management along with corticosteroids, as that being followed in our set-up, for a faster recovery with minimal complications.

However, long term study with larger sample size is needed to validate the modified SCORTEN proposed by us.

SUMMARY

The inferences derived from this prospective study done on Stevens-Johnson syndrome and Toxic Epidermal Necrolysis patients, attending Dermatology department and Intensive Medical Care Unit, Tirunelveli Medical College Hospital are as follows:

- The incidence of SJS and TEN among other drug reactions was 29.5%.
- The most common age group affected was 30-49 years (41.1%), with a mean age of 39.2±18.4 years in males and 35.5±24.7 years in females.
- There was a male preponderance in the study with male: female ratio being 3.25 : 1.
- The most common spectrum in our study is TEN followed by SJS and SJS-TEN Overlap on the basis of Bastuji-Garin et al classification.
- Prodromal symptoms were present in 70.6% of cases, prior to the onset of cutaneous lesions.
- The disease began from the skin in 41.7 % of cases, whereas in 47%, mucosal lesions preceded the skin lesions and in 11.8%, simultaneous onset of lesions occured.
- A positive history of drug intake was present in 100% of patients. Single etiological agent was identified in 94.1%.

- Anticonvulsants were the commonest drugs implicated in 47% of patients, followed by analgesics and antibiotics in 35% and 11% of cases respectively. In 1 patient, antitubercular therapy (Category I) was found as the cause of reaction. Causative agent could not be determined in 5.9% of patients due to lack of adequate drug details.
- In majority of patients (64.7%), the lesions started within 3 weeks of drug administration with mean of 16 days. The mean duration between drug administration and disease onset was higher for anticonvulsants and shorter for analgesics.
- Past history of similar illness was encountered in 3 patients. In case of analgesics (2 patients), the second episode occurred earlier and more severe than the first episode. But in case of anticonvulsants (1 patient), the second episode took a longer time and was milder than the first episode. Owing to the small case number, statistically significant conclusions could not be derived from this.
- The predominant site of skin lesions were the trunk and proximal extremities in 70.6% of cases.
- Morphologically, the skin lesions were necrotic epidermis and erosions in 70.58%, followed by vesicles and bulla in 47.1% of patients.

- Mucosal involvement was present in all patients. The predominant mucosal sites involved were the oral and urogenital in 100% and 76.5% of cases respectively.
- Nikolsky skin was positive in 82.4% of cases.
- Most of the patients had deranged hematological (47%) and biochemical parameters(29.4%). Liver enzymes were raised in 35.3% of cases whereas, renal parameters were elevated in 17.6% of cases.
- All patients who suffered mortality, had thrombocytopenia and elevation of blood urea nitrogen. But pneumonitis in chest X-ray and elevated liver enzymes were found in 2 of 3 patients who succumbed to death.
- Septicemia was confirmed in 1 patient with positive blood culture.
- Co- morbidities were present in 70.6% of patients. This includes, epilepsy and cerebrovascular accident in 41.2% of patients, diabetes and chronic kidney disease in 11.8% of patients. Carcinoma lung and systemic lupus erythematosus were encountered in 5.88% of patients. No cardiovascular co-morbidity was noted in our study.
- Out of 17 patients, 3(17.6%) died, which included 2 patients of SJS-TEN Overlap and 1 case of TEN.

- SCORTEN scoring showed significant positive correlation between predicted mortality and observed mortality on day 1, 3 and 5. A higher score was associated with higher mortality.
- On comparing SCORTEN values between live patients and dead patients, the dead patients had relatively higher scores and the difference was statistically significant.
- On univariate analysis, BUN elevation was highly associated with mortality followed by RBS >252mg/dl and tachycardia. Whereas, age, serum bicarbonate, % body surface area detachment had no significant effect on mortality.
- Some other possible prognostic factors not included in SCORTEN were also analysed. Factors which were significantly associated with mortality were co-existent morbidity especially CKD, thrombocytopenia and pneumonitis.
- It was also seen that increased body surface area involvement did not correlate much with the mortality in our study. Since the patients with 100% BSA involvement with no co-morbidity recovered well.
- A conservative line of management along with steroids was followed for all patients and majority of them recovered rapidly with minimal complications.

TOXIC EPIDERMAL NECROLYSIS TO CARBAMAZEPINE IN A SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT

AFTER 1YEAR

SHEET OF EPIDERMAL DETACHMENT

TOXIC EPIDERMAL NECROLYSIS TO ANALGESIC IN A PLHA PATIENT

DAY 1-EPIDERMAL NECROSIS WITH FISSURING AND PURULENT CRUSTING ENTIRE BODY WITH HEMORRHAGIC CRUSTING LIPS, CONJUNCTIVAL INVOLVEMENT

DAY 6-SHEETS OF EPIDERMAL DETACHMENT IN RESOLVING TEN

DAY 10 - RECOVERED SKIN AND HEALING MUCOSAL LESIONS

SCALP INVOLVEMENT

STEVENS-JOHNSON SYNDROME

PALPABREL AND BULBAR CONJUNCTIVAL EROSIONS

EROSION IN THE NOSE AND TARGETOID LESIONS

EROSION WITH CRUSTING OF LIPS

PALATAL AND OROPHARYNX EROSIONS

EPIDERMAL DETACHMENT INVOLVING MONS PUBIS

EROSION OF GLANS PENIS

A CASE OF SECOND EPISODE OF TEN TO ANALGESIC

DAY 1

DAY 3

DAY 5 - RAPID RECOVERY IN CASE OF SECOND EPISODE

AT THE END OF 1 MONTH - POST INFLAMMMATORY HYPERPIGMENATION

CASE OF TEN TO RECTAL PARACETAMOL TREATED WITH IVIG

DAY 1

LESIONS PROGRESSED ON DAY 4

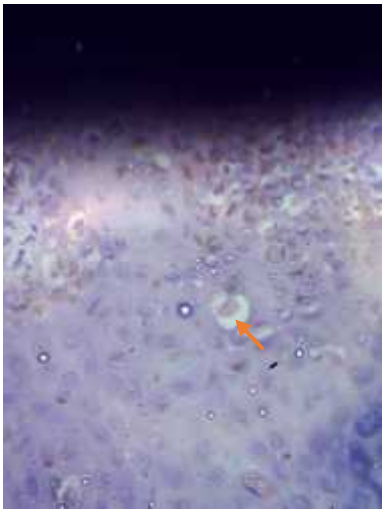
DAY 12 - AFTER TREATMENT WITH IVIG

TARGETOID LESION IN TEN

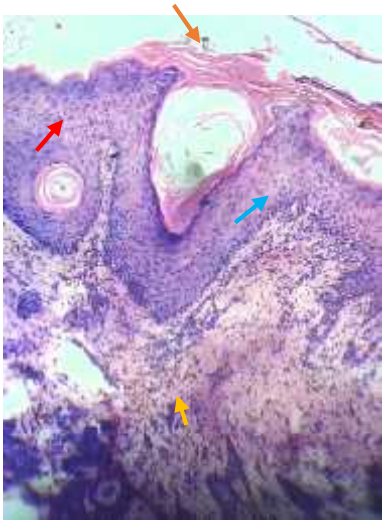
NIKOLSKY SIGN

IRIS OF BATEMAN LESIONS IN A SJS-TEN OVERLAP

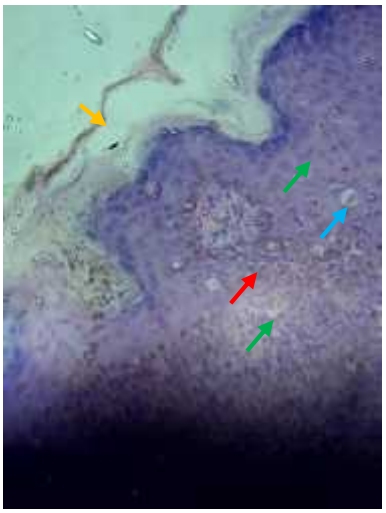
HISTOPATHOLOGY



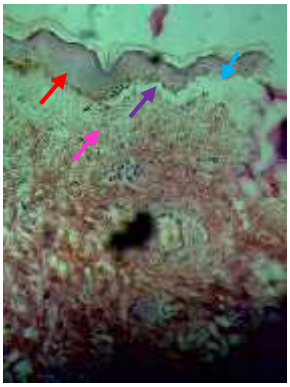
↗**APOPTOTIC KERATINOCYTES - 40X**



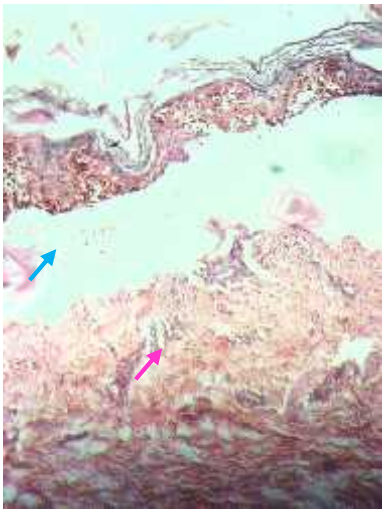
↗**HYPERKERATOSIS & FOLLICULAR PLUGGING**
↗**ACANTHOSIS**
↗**SPONGIOSIS**
↗**MELANIN INCONTINENCE**



INTRAEPIDERMAL CLEFT
NECROTIC KERATINOCYTES
CIVATTE BODIES
SPONGIOSIS



SUBEPIDERMAL BULLA
VACUOLISATION OF BASAL CELL
SPONGIOSIS
DILATED BLOOD VESSELS IN DERMIS



↗**SUBEPIDERMAL CLEFTING**
↗**PERIVASCULAR INFILTRATE**

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S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
1	Mariappan	39	M	TEN	red spots, blistering, skin pain, painful oral lesion	3	itch	1 DAY	malaise, conjunctivitis	CVA	**T. PHENYTOIN,** T. IBUPROFEN, C. CEPHALEXIN	POST HEAD INJURY, CVA	28DAYS	NECROTIC EPIDERMIS, VESICLES, BULLA	entire body except scalp & distal extremities
2	Nayagam	39	F	TEN (2nd Episode)	blistering, skin pain	2	itch, burning sensation	12HOURS	URI	NO	**T.ANACIN,** C. AMOXYCILLIN	URTI. OTC INTAKE	1 DOSE	NECROTIC EPIDERMIS, VESICLES, BULLA	entire body except face, scalp, distal extremities

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
3	Abdul jaleel	18	M	TEN	red spots, blistering, skin pain, painful oral lesion,painful oral lesion	1	NIL	NA	NIL	EPILEPSY	**T. CARBAMAZEPINE**	EPILEPSY/CPS	5DAYS	NECROTIC EPIDERMIS, TARGETOID LESION	entire body except scalp & distal extremities
4	Paul	49	M	TEN	skin peeling, black discolouration, skin pain, painful oral lesion	3	NIL	NA	NIL	PLHA	**UNIDENTIFIED ANALGESIC**	OTC FOR LEG PAIN	7DAYS	NECROTIC EPIDERMIS, PURULENT CRUST	entire body except distal extremities

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
5	Jeganraja	22	M	SJS	painful oral lesion	4	itch	6 DAYS	fever , malaise	NO	**T.ACECLOFENAC,** T.CEFIXIME	FEVER	2DAYS	NECROTIC EPIDERMIS	lips
6	Venkatesh	19	M	TEN	red spots, painful oral lesion	6	itch	2 DAYS	NIL	PTB	HREZ	PTB	40DAYS	NECROTIC EPIDERMIS	entire body except scalp & distal extremities

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
7	Thillai	43	M	TEN	peeling, red spots, blistering, black discolor ,painful oral lesion	3	NIL	NA	fever ,malaise,conjunctivitis	EPILEPSY, CA LUNG	**T.PHENYTOIN,** T.PARACETAMOL	EPILEPSY DUE TO BRAIN SECONDARY	26DAYS	NECROTIC EPIEPIDERMIS, VESICLE, BULLA	entire body except scalp & distal extremities

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
8	Natarajan	67	M	TEN (2nd Episode)	blistering, black discoloration	4	burning	30 minutes	NIL	NO	**T.IBUPROFEN**	OTC INTAKE FOR BODYACHE	1 DOSE	NECROPTIC EPIDERMIS, BULLA	entire body except face,scalp & distal extremities

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
9	Perumal	61	M	SJS	skin peeling, painful oral lesion, eye redness and pain	6	NIL	NA	malaise	NO	CEPHALEXIN, **SIGNOFLAM**	OTC FOR UTI	10 DAYS	VESICLES, NECROTIC EPIDERMIS	abdomen, genitals, thighs, gluteal
10	Mupidathi	65	F	SJS - TEN Overlap	red spots	5	NIL	NA	NIL	EPILEPSY, DM, HYPOTHYROIDISM	**CARBAMAZEPINE** , GLIMIPIRIDE, METFORMIN,	EPILEPSY	15 DAYS	NECROTIC EPIDERMIS	entire body except face,scalp & distal extremities

12	11	**S. NO.**
madasamy	Porselvi	**NAME**
35	6	**AGE**
M	FCH	**SEX**
TEN	TEN	**DIAGNOSIS**
blistering, black discoloration, skin pain,painful oral lesion	blistering, black discoloration, skin pain,painful oral lesion	**COMPLAINTS**
3	3	**DURATION (DAYS)**
skin pain	NIL	**PRODROME**
4days	NA	**DURATION OF PRODROME**
URI, conjunctivitis	fever	**SYSTEMIC SYMP**
CVA	NO	**COMORBIDITIES**
T. PHENYTOIN, ANALGESIC, ANTIBIOTIC	Inj paracetamol, **inj ampicillin**	**DRUG HISTORY**
POST HEAD INJURY-CVA	FEVER	**INDICATION**
31 DAYS	3DAYS	**DURATION**
NECROTIC EPI, VESICLE, BULLA, TARGETOID	NECROTIC EPIEPIDERMIS, BULLA, EROSION	**MORPHOLOGY**
trunk,arm,genitals	entire body except scalp	**SITE(SKIN)**

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
13	thangaraj	45	M	SJS-TEN Overlap	black discoloration,skin pain,painful oral lesion	5	NIL	NA	fever, malaise, URI	DM, CKD, CAD	**T.NORFLOX,** T.METRO, T.PARA, T.MF, INJ HA	FEVER	7DAYS	NECROTIC EPIDERMIS	entire body except scalp & distal extremities
14	maharaja	65	M	SJS-TEN Overlap	painful oral, lip and genital lesion, red spots,eye redness and pain	5	itch	5days	fever , malaise,cough	CVA/ CKD	**t.phenytoin,** t.atorvostatin, t.amlodipine, t.lasix	POST HEAD INJURY-CVA	40 DAYS	NECROTIC EPIDERMIS, TARGETOID	FACE, TRUNK

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
15	madasamy	35	M	SJS (2nd Episode)	painful oral and lip lesion,eye redness and pain	3	NIL	NA	NIL	CVA	**t. phenytoin**	POST HEAD INJURY-CVA	40 DAYS	HAEMORRHAGIC LIP CRUSTING, CONJUNCTIVAL CONGESION, TARGETOID	lips,oral mucosa & eyes

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
16	Valli	27	F	TEN	skin peeling, pain,painful oral lesion,eye redness and pain	3	skin pain	1 day	fever, malaise	LUPUSNEPHRITIS	PREDNISOLONE, **T.CARBAMAZEPINE**	LUPUS/OTC	15 DAYS	NECROTIC EPIDERMIS, VESICLE, BULLA	entire body except lowerlimb and scalp

S. NO.	NAME	AGE	SEX	DIAGNOSIS	COMPLAINTS	DURATION (DAYS)	PRODROME	DURATION OF PRODROME	SYSTEMIC SYMP	COMORBIDITIES	DRUG HISTORY	INDICATION	DURATION	MORPHOLOGY	SITE(SKIN)
17	Esakimuthu	11	MCH	TEN	blistering, blackish discolouration, skin pain, painful oral lesion	3	Skin pain	1 day	fever, malaise, cough	NO	syrup erythromycin, syrup pheniramine maleate, **rectal suppository ofparacetamol**	fever	6 DAYS	NECROTIC EPIDERMIS, VESICLE, BULLA, TARGETOID	entire body except scalp

2	1	**S. NO.**
Nayagam	Mariappan	**NAME**
YES	YES	**NIKOLSKY**
oral, urogenital	oral, conj, pharnyx, urogenitals	**mucosa**
DIFFUSE ERYTHEMA	NORMAL	**PALMS & SOLES**
NO	NO	**SCALP & HAIR**
NO	NO	**NAILS**
10	8	**RECOVERY TIME SKIN (DAYS)**
7	7	**RECOVERY TIME MUCOSA (DAYS)**
N	LEUKOPENIA	**CBC**
N	N	**LFT**
N	N	**RFT**
N	N	**C&S**
NRL	NRL	**CXRAY**
NO	NO	**AGE >40 YEARS**
NO	NO	**CA**
NO	NO	**DAY 1 HR >120**
NO	NO	**DAY 3 HR >120**
NO	NO	**DAY 5 HR >120**
YES	YES	**DAY 1 EPIDERMAL**
NO	NO	**DAY 1 BUN >28%**
NO	NO	**DAY 3 BUN >28%**
NO	NO	**DAY 5 BUN >28%**
NO	NO	**DAY 1 RBS**
NO	NO	**DAY 3 RBS**
NO	NO	**DAY 5 RBS**
NO	YES	**DAY 1 Se HCO3 <20mmol/l**
YES	YES	**DAY 3 Se HCO3 <20mmol/l**
NO	NO	**DAY 5 Se HCO3 <20mmol/l**
1	2	**DAY 1 SCORTEN**
2	2	**DAY 3 SCORTEN**
1	1	**DAY 5 SCORTEN**
iv dexamethasone	iv dexamethasone	**TREATMENT**
NO	NO	**MORTALITY-COD**
pigmentary change, dry eyes	pigmentary changes	**FOLLOW UP CHANGE**

4	3	S. NO.
Paul	Abdul jaleel	NAME
YES	YES	NIKOLSKY
oral,conj,nasal,pharynx,urogenital,anal	oral, conj, urogenitals	mucosa
DIFFUSE ERYTHEMA	ERYTHEMATOUS MACULES	PALMS & SOLES
YES	NO	SCALP & HAIR
NO	NO	NAILS
14	10	RECOVERY TIME SKIN (DAYS)
7	7	RECOVERY TIME MUCOSA (DAYS)
ANAEMIA,LEUKOCYTOSIS	LEUKOCYTOSIS	CBC
N	N	LFT
N	N	RFT
STAPH AUREUS(SKIN C&S)	N	C&S
NRL	NRL	CXRAY
YES	NO	AGE >40 YEARS
NO	NO	CA
NO	NO	DAY 1 HR >120
NO	NO	DAY 3 HR >120
NO	NO	DAY 5 HR >120
YES	YES	DAY 1 EPIDERMAL
NO	NO	DAY 1 BUN >28%
NO	NO	DAY 3 BUN >28%
NO	NO	DAY 5 BUN >28%
NO	NO	DAY 1 RBS
NO	NO	DAY 3 RBS
NO	NO	DAY 5 RBS
YES	NO	DAY 1 Se HCO3 <20mmol/l
YES	YES	DAY 3 Se HCO3 <20mmol/l
YES	NO	DAY 5 Se HCO3 <20mmol/l
3	1	DAY 1 SCORTEN
3	2	DAY 3 SCORTEN
3	1	DAY 5 SCORTEN
iv dexamethasone	iv dexamethasone	TREATMENT
NO	NO	MORTALITY-COD
pigmentary changes	pigmentary changes	FOLLOW UP CHANGE

6	5	S. NO.
Venkatesh	Jeganraja	NAME
YES	NO	NIKOLSKY
oral, urogenital	oral	mucosa
NORMAL	NORMAL	PALMS & SOLES
NO	NO	SCALP & HAIR
NO	NO	NAILS
14	NA	RECOVERY TIME SKIN (DAYS)
21	10	RECOVERY TIME MUCOSA (DAYS)
LEUKOCYTOSIS	N	CBC
N	N	LFT
N	N	RFT
N	N	C&S
NRL	NRL	CXRAY
NO	NO	AGE >40 YEARS
NO	NO	CA
NO	NO	DAY 1 HR >120
NO	NO	DAY 3 HR >120
NO	NO	DAY 5 HR >120
YES	NO	DAY 1 EPIDERMAL
NO	NO	DAY 1 BUN >28%
NO	NO	DAY 3 BUN >28%
NO	NO	DAY 5 BUN >28%
NO	NO	DAY 1 RBS
NO	NO	DAY 3 RBS
NO	NO	DAY 5 RBS
NO	YES	DAY 1 Se HCO3 <20mmol/l
YES	NO	DAY 3 Se HCO3 <20mmol/l
NO	YES	DAY 5 Se HCO3 <20mmol/l
1	1	DAY 1 SCORTEN
2	1	DAY 3 SCORTEN
1	1	DAY 5 SCORTEN
iv dexamethasone	iv dexamethasone	TREATMENT
NO	NO	MORTALITY-COD
pigmentary change	NO	FOLLOW UP CHANGE

7	**S. NO.**
Thillai	**NAME**
YES	**NIKOLSKY**
oral, urogenital	**mucosa**
PURPURA AND PETECHIA	**PALMS & SOLES**
NO	**SCALP & HAIR**
NO	**NAILS**
NA	**RECOVERY TIME SKIN (DAYS)**
NA	**RECOVERY TIME MUCOSA (DAYS)**
THROMBOCYTOPENIA	**CBC**
N	**LFT**
elevated	**RFT**
STAPH.AUREUS(BLOOD C&S), KLEBSIELLA(SKIN C&S)	**C&S**
INFILTRATES +	**CXRAY**
YES	**AGE >40 YEARS**
YES	**CA**
YES	**DAY 1 HR >120**
YES	**DAY 3 HR >120**
YES	**DAY 5 HR >120**
YES	**DAY 1 EPIDERMAL**
YES	**DAY 1 BUN >28%**
YES	**DAY 3 BUN >28%**
YES	**DAY 5 BUN >28%**
NO	**DAY 1 RBS**
NO	**DAY 3 RBS**
YES	**DAY 5 RBS**
YES	**DAY 1 Se HCO3 <20mmol/l**
YES	**DAY 3 Se HCO3 <20mmol/l**
YES	**DAY 5 Se HCO3 <20mmol/l**
6	**DAY 1 SCORTEN**
6	**DAY 3 SCORTEN**
7	**DAY 5 SCORTEN**
iv dexamethasone	**TREATMENT**
YES- ARDS, SEPSIS	**MORTALITY-COD**
NA	**FOLLOW UP CHANGE**

8	**S. NO.**
Natarajan	**NAME**
YES	**NIKOLSKY**
oral, urogenital	**mucosa**
NORMAL	**PALMS & SOLES**
NO	**SCALP & HAIR**
NO	**NAILS**
9	**RECOVERY TIME SKIN (DAYS)**
7	**RECOVERY TIME MUCOSA (DAYS)**
LEUKOCYTOSIS	**CBC**
N	**LFT**
N	**RFT**
N	**C&S**
NRL	**CXRAY**
YES	**AGE >40 YEARS**
NO	**CA**
NO	**DAY 1 HR >120**
NO	**DAY 3 HR >120**
NO	**DAY 5 HR >120**
YES	**DAY 1 EPIDERMAL**
NO	**DAY 1 BUN >28%**
NO	**DAY 3 BUN >28%**
NO	**DAY 5 BUN >28%**
NO	**DAY 1 RBS**
NO	**DAY 3 RBS**
NO	**DAY 5 RBS**
NO	**DAY 1 Se HCO3 <20mmol/l**
NO	**DAY 3 Se HCO3 <20mmol/l**
YES	**DAY 5 Se HCO3 <20mmol/l**
2	**DAY 1 SCORTEN**
2	**DAY 3 SCORTEN**
2	**DAY 5 SCORTEN**
iv dexamethasone	**TREATMENT**
NO	**MORTALITY-COD**
pigmentary changes, Palmoplantar psoriasis	**FOLLOW UP CHANGE**

10	9	**S. NO.**
Mupidathi	Perumal	**NAME**
NO	YES	**NIKOLSKY**
oral	oral, conj,nasal,pharynx,urogenital	**mucosa**
ERYTHEMATOUS MACULES	NORMAL	**PALMS & SOLES**
NO	NO	**SCALP & HAIR**
NO	NO	**NAILS**
10	15	**RECOVERY TIME SKIN (DAYS)**
14	4	**RECOVERY TIME MUCOSA (DAYS)**
LEUKOCYTOSIS	N	**CBC**
N	N	**LFT**
N	N	**RFT**
N	N	**C&S**
NRL	NRL	**CXRAY**
YES	YES	**AGE >40 YEARS**
NO	NO	**CA**
NO	NO	**DAY 1 HR >120**
NO	NO	**DAY 3 HR >120**
NO	NO	**DAY 5 HR >120**
NO	YES	**DAY 1 EPIDERMAL**
NO	NO	**DAY 1 BUN >28%**
NO	NO	**DAY 3 BUN >28%**
NO	NO	**DAY 5 BUN >28%**
NO	NO	**DAY 1 RBS**
NO	NO	**DAY 3 RBS**
NO	NO	**DAY 5 RBS**
YES	YES	**DAY 1 Se HCO3 <20mmol/l**
YES	YES	**DAY 3 Se HCO3 <20mmol/l**
NO	YES	**DAY 5 Se HCO3 <20mmol/l**
3	3	**DAY 1 SCORTEN**
3	3	**DAY 3 SCORTEN**
2	4	**DAY 5 SCORTEN**
iv dexamethasone	iv dexamethasone	**TREATMENT**
NO	NO	**MORTALITY-COD**
pigmentary change, dry eyes	pigmentary changes	**FOLLOW UP CHANGE**

12	11	**S. NO.**
madasamy	Porselvi	**NAME**
YES	YES	**NIKOLSKY**
oral,conj,urogenital,	oral, nasal, conjunctival, pharynx, urogenital	**mucosa**
NORMAL	ERYTHEMATOUS MACULES	**PALMS & SOLES**
NO	NO	**SCALP & HAIR**
NO	NO	**NAILS**
9	7	**RECOVERY TIME SKIN (DAYS)**
12	14	**RECOVERY TIME MUCOSA (DAYS)**
LEUKOCYTOSIS	LEUKOPENIA	**CBC**
N	SGOT, SGPT INCREASED	**LFT**
N	N	**RFT**
N	N	**C&S**
NRL	NRL	**CXRAY**
NO	NO	**AGE >40 YEARS**
NO	NO	**CA**
NO	NO	**DAY 1 HR >120**
NO	NO	**DAY 3 HR >120**
NO	NO	**DAY 5 HR >120**
YES	YES	**DAY 1 EPIDERMAL**
NO	NO	**DAY 1 BUN >28%**
NO	NO	**DAY 3 BUN >28%**
NO	NO	**DAY 5 BUN >28%**
NO	NO	**DAY 1 RBS**
NO	NO	**DAY 3 RBS**
NO	NO	**DAY 5 RBS**
YES	NO	**DAY 1 Se HCO3 <20mmol/l**
NO	YES	**DAY 3 Se HCO3 <20mmol/l**
YES	NO	**DAY 5 Se HCO3 <20mmol/l**
2	1	**DAY 1 SCORTEN**
1	2	**DAY 3 SCORTEN**
2	1	**DAY 5 SCORTEN**
iv dexamethasone	INJ DEXAMETHASONE	**TREATMENT**
NO	NO	**MORTALITY-COD**
pigmentary changes	pigmentary change	**FOLLOW UP CHANGE**

14	13	S. NO.
maharaja	thangaraj	NAME
YES	YES	NIKOLSKY
conj,nasal,oral,pharynx,urogenital	oral, conj,nasal,pharynx,urogenital	mucosa
DIFFUSE ERYTHEMA AND BULLA	NORMAL	PALMS & SOLES
NO	YES	SCALP & HAIR
NO	NO	NAILS
NA	7	RECOVERY TIME SKIN (DAYS)
	NA	RECOVERY TIME MUCOSA (DAYS)
ANAMIA, THROMBOCYTOPENIA	ANAEMIA,	CBC
SGOT,SGPT INCREASED	SGPT,ALP INCREASED	LFT
elevated	elevated	RFT
N	N	C&S
INFILTRATES +	NRL	CXRAY
YES	YES	AGE >40 YEARS
NO	NO	CA
NO	NO	DAY 1 HR >120
NO	NO	DAY 3 HR >120
YES	NO	DAY 5 HR >120
YES	YES	DAY 1 EPIDERMAL
NO	YES	DAY 1 BUN >28%
YES	YES	DAY 3 BUN >28%
YES	YES	DAY 5 BUN >28%
NO	YES	DAY 1 RBS
NO	YES	DAY 3 RBS
NO	YES	DAY 5 RBS
YES	YES	DAY 1 Se HCO3 <20mmol/l
YES	YES	DAY 3 Se HCO3 <20mmol/l
YES	YES	DAY 5 Se HCO3 <20mmol/l
4	5	DAY 1 SCORTEN
4	5	DAY 3 SCORTEN
5	5	DAY 5 SCORTEN
iv dexamethasone	iv dexamethasone	TREATMENT
YES-AKI ON CKD	YES-AKI ON CKD/DKA	MORTALITY-COD
NA	NA	FOLLOW UP CHANGE

15	**S. NO.**
madasamy	**NAME**
NO	**NIKOLSKY**
ORAL, NASAL, CONJUNCTIVAL, PHARYNX	**mucosa**
NO	**PALMS & SOLES**
NO	**SCALP & HAIR**
NO	**NAILS**
NA	**RECOVERY TIME SKIN (DAYS)**
	RECOVERY TIME MUCOSA (DAYS)
N	**CBC**
SGOT, SGPT INCREASED	**LFT**
N	**RFT**
N	**C&S**
NRL	**CXRAY**
NO	**AGE >40 YEARS**
NO	**CA**
NO	**DAY 1 HR >120**
NO	**DAY 3 HR >120**
NO	**DAY 5 HR >120**
NO	**DAY 1 EPIDERMAL**
NO	**DAY 1 BUN >28%**
NO	**DAY 3 BUN >28%**
NO	**DAY 5 BUN >28%**
NO	**DAY 1 RBS**
NO	**DAY 3 RBS**
NO	**DAY 5 RBS**
YES	**DAY 1 Se HCO3 <20mmol/l**
YES	**DAY 3 Se HCO3 <20mmol/l**
YES	**DAY 5 Se HCO3 <20mmol/l**
1	**DAY 1 SCORTEN**
1	**DAY 3 SCORTEN**
1	**DAY 5 SCORTEN**
iv dexamethasone	**TREATMENT**
NO	**MORTALITY-COD**
pigmentary change, dry eyes	**FOLLOW UP CHANGE**

16	**S. NO.**
Valli	**NAME**
YES	**NIKOLSKY**
oral,conj,nasal,pharynx,urogenital,anal	**mucosa**
PURPURA AND PETECHIA	**PALMS & SOLES**
NO	**SCALP & HAIR**
NO	**NAILS**
14	**RECOVERY TIME SKIN (DAYS)**
14	**RECOVERY TIME MUCOSA (DAYS)**
N	**CBC**
SGOT, SGPT INCREASED	**LFT**
N	**RFT**
N	**C&S**
NRL	**CXRAY**
NO	**AGE >40 YEARS**
NO	**CA**
NO	**DAY 1 HR >120**
NO	**DAY 3 HR >120**
NO	**DAY 5 HR >120**
YES	**DAY 1 EPIDERMAL**
NO	**DAY 1 BUN >28%**
NO	**DAY 3 BUN >28%**
NO	**DAY 5 BUN >28%**
NO	**DAY 1 RBS**
NO	**DAY 3 RBS**
NO	**DAY 5 RBS**
YES	**DAY 1 Se HCO3 <20mmol/l**
YES	**DAY 3 Se HCO3 <20mmol/l**
YES	**DAY 5 Se HCO3 <20mmol/l**
2	**DAY 1 SCORTEN**
2	**DAY 3 SCORTEN**
2	**DAY 5 SCORTEN**
iv dexamethasone	**TREATMENT**
NO	**MORTALITY-COD**
pigmentary changes, dry eyes	**FOLLOW UP CHANGE**

17	**S. NO.**
Esakimuthu	**NAME**
YES	**NIKOLSKY**
oral,conj,nasal,pharynx,urogenital,anal	**mucosa**
PURPURA AND PETECHIA	**PALMS & SOLES**
NO	**SCALP & HAIR**
NO	**NAILS**
14	**RECOVERY TIME SKIN (DAYS)**
18	**RECOVERY TIME MUCOSA (DAYS)**
N	**CBC**
SGOT,SGPT INCREASED	**LFT**
	RFT
N	**C&S**
INFILTRATES +	**CXRAY**
	AGE >40 YEARS
NO	**CA**
NO	**DAY 1 HR >120**
NO	**DAY 3 HR >120**
NO	**DAY 5 HR >120**
YES	**DAY 1 EPIDERMAL**
NO	**DAY 1 BUN >28%**
NO	**DAY 3 BUN >28%**
NO	**DAY 5 BUN >28%**
NO	**DAY 1 RBS**
NO	**DAY 3 RBS**
NO	**DAY 5 RBS**
YES	**DAY 1 Se HCO3 <20mmol/l**
YES	**DAY 3 Se HCO3 <20mmol/l**
YES	**DAY 5 Se HCO3 <20mmol/l**
2	**DAY 1 SCORTEN**
2	**DAY 3 SCORTEN**
2	**DAY 5 SCORTEN**
Inj Dexamethasone and IVIG	**TREATMENT**
NO	**MORTALITY-COD**
pigmentary changes, dry eyes	**FOLLOW UP CHANGE**

ABBREVIATION

SJS – Stevens-Johnson Syndrome

TEN – Toxic Epidermal Necrolysis

SCORTEN – SCORing system for Toxic Epidermal Necrolysis

EMF – Erythema multiforme

SCAR – Severe Cutaneous Adverse Reactions

ADR – Adverse drug reactions

DRESS - drug related eosinophilia and systemic symptoms(DRESS)

AGEP - acute generalized exanthematous pustulosis

HMGB1 - high mobility group protein B1

LFT – Liver function test

RFT – Renal function test

GVHD – Graft vs Host Diseases

ARDS – Acute respiratory distress syndrome

PROFORMA

Name: Case no:

Age: Date:

Sex

Residence:

Occupation:

DOA:

DOD/DOE:

HISTORY:

Presenting complaint:

Duration:

Onset and Progression:

h/o epidermal detachment: yes/no

h/o mucosal involvement: oral/conjunctival/nasal/pharyngeal/genital/urethral/anal

h/o fever: yes/no

h/o prodromal symptoms: malaise/ sore throat/ cough/ coryza/ conjunctivitis/ myalgia/ arthralgia/ pruritus

h/o chest pain: yes/no

h/o dyspnea: yes/no

h/o diarrhea, melena

h/o abdominal distention/constipation/vomiting

h/o hematuria

h/o difficulty in opening the eyes

h/o possible etiologies:

h/o sore throat/cough/dyspnea (mycoplasma pneumonia)

h/s/o herpes simplex

h/o vaccination in the recent past

h/o organ transplantation

h/o predisposing factors:

h/s/o systemic lupus erythematosus/ other connective tissue disorder

k/c/o malignancy

k/c/o HIV

k/c/o rheumatologic disorder

past h/o similar illness

past history

k/c/o DM/HT/BA/Epilepsy/Tb/jaundice

others:

h/o alcoholism / smoking

exposure history:

family h/o similar illness

DETAILS OF DRUG TAKEN DURING PRECEDING 3 WEEKS

SNO	NAME OF DRUG	DATE	
		FROM	TO

EXAMINATION

GENERAL EXAMINATION

Conscious

Oriented

Comfortable at rest

Pallor

Jaundice

Cyanosis

Generalized lymphadenopathy

VITALS:

PR:

BP:

RR:

Temp:

I/O

DERMATOLOGICAL EXAMINATION

SKIN TENDERNESS:

PSEUDO NIKOLSKY SIGN:

ORAL EXAMINATION

GENITAL EXAMINATION

PALMS & SOLES

SCALP & HAIR

OPTHALMOLOGICAL EXAMINATION

SCORTEN ANALYSIS

RISK FACTORS	DAY 1	DAY 2	DAY 3
Age above 40 years			
Presence of malignancy			
Tachycardia (heart rate > 120bpm)			
Epidermal detachment above 10%			
Blood urea nitrogen > 28mg/dl			
Serum glucose level > 252mg/dl			
Bicarbonate level <20mmol/l			

TOTAL SCORE

DAY 1

DAY 3

DAY 5

INVESTIGATIONS

Urine- Albumin

Sugar

Deposits

Hb

TC

DC

ESR

Platelet count

RBS

Urea

Creatinine

Se Na++

Se K+

HCO3

Total bilirubin

SGOT

SGPT

ALP

Total protein

Albumin

Globulin

Peripheral smear study

HIV

VDRL

Urine C & S

Blood C & S

Skin swab C & S

Throat swab C & S

Stool for occult blood

Chest x ray

Ecg in all leads

USG abdomen & pelvis

Tzanck smear

Skin biopsy

DIF

TREATMENT

EXAMINATION AT FOLLOW UP

OCULAR EXAMINATION: dry eyes/others

NAILS: pigmentation/ ridging/ dystrophy/ permenant anychia

GENITAL:

Vulvovaginal: dryness/scarring

Phimosis

Esophageal / urethral/ anal stricture

Joint contracture

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பத்தற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்டஅறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
ஆய்வாளரின் பெயர் .....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....